Volume 30 No. 12 December, 1960

JOURNAL OF GENERAL CHEMISTRY of the USSR

ЖУРНАЛ ОБЩЕЙ ХИМИИ
(ZHURNAL OBSHCHEI KHIMII)

TRANSLATED FROM RUSSIAN

CONSULTANTS BUREAU

Volume 30, No. 12
December, 1960

JOURNAL OF
GENERAL CHEMISTRY
OF THE USSR

(ZHURNAL OBSHCHEI KHIMII)

A publication of the Academy of Sciences of the USSR

IN ENGLISH TRANSLATION

Year and issue of first translation:
Vol. 19 No. 1 January 1949

	U. S. and Canada	*Foreign*
Annual Subscription	*$120.00*	*$125.00*
Annual subscription for libraries of nonprofit academic institutions	*50.00*	*55.00*
Single issue	*15.00*	*15.00*

Printed in the United States of America

JOURNAL OF GENERAL CHEMISTRY OF THE USSR

Volume 30, Number 12 December, 1960

CONTENTS

CONTENTS (continued)

CONTENTS (continued)

HEATS OF SOLUTION OF THE HEXAHYDRATES OF CADMIUM AND MERCURY PERCHLORATES

S. A. Shchukarev, Z. U. Borisova, and A. M. Gusev

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3857-3859, December, 1960
Original article submitted February 4, 1960

The heats of solution of the hexahydrates of cadmium and mercury perchlorates have been determined as in our previous studies [1, 2]. Cadmium perchlorate hexahydrate, which was prepared by dissolving cadmium carbonate in perchloric acid, was recrystallized 5 times. The hexahydrate obtained was freed of excess mother liquor by drying in a manipulator over concentrated sulfuric acid. The degree of drying was controlled by parallel analysis of the hexahydrate for cadmium and ClO_4^- and simultaneous determination of its heat of solution. The analysis for cadmium was made by titrating with Trilon B, with Acid Chrome Dark Blue as the indicator. The accuracy of the analysis was ±0.03%. The ClO_4^- content was determined in the same manner as previously [3]. The maximum endoeffect of solution was obtained for cadmium perchlorate containing 6.00 molecules of water per mole of anhydrous salt.

Found %: Cd 26.81; Cl 16.88. $Cd(ClO_4)_2 \cdot 6H_2O$. Calculated %: Cd 26.80; Cl 16.19.

The heats of solution in water of cadmium perchlorate were determined for the following dilutions (in moles per mole): 1 : 1000, 1 : 700, 1 : 500, 1 : 200, 1 : 100, 1 : 50, 1 : 30, 1 : 20, 1 : 13, 1 : 10, and 1 : 6.7. The heats of solution for dilutions from 1 : 1000 to 1 : 30 were determined directly by solution of a weighed sample of cadmium perchlorate hexahydrate in water. For dilutions of 1 : 20 and less, intermediate heats of solution were determined. The cadmium perchlorate hexahydrate was dissolved not in water, but in a solution of the perchlorate of definite concentration, the heat of solution of which was known. The average values obtained from 7-8 experiments are given in Table 1.

The concentration of a saturated solution of cadmium perchlorate at 25° is 4.41 moles of anhydrous perchlorate per 1000 g of water [4]. Thus the last dilution (1 : 6.7) for which we determined the heat of solution differs from the saturated solution by 0.2 mole of water.

Preparation of mercury perchlorate hexahydrate with the stoichiometric proportions of the components presented considerable difficulty. Mercury perchlorate in aqueous solutions undergoes considerable hydrolysis (according to the data of [5], a 5.51 molal solution of the perchlorate has a pH of 1.56). On recrystallization from aqueous solutions, therefore, hexahydrate contaminated with basic salts is obtained. Such a preparation gives low values for the heat of solution in water. On the other hand, on recrystallization from solutions of perchloric acid of appreciable concentration the hexahydrate precipitates out containing an excess of perchloric acid. The presence of the excess perchloric acid in the hexahydrate also lowers the endoeffect of solution of the mercury perchlorate hexahydrate in water. The recrystallization of the hexahydrate therefore was carried out from solutions of perchloric acid of such a concentration (~ 2 N) that mercury perchlorate hexahydrate precipitated with the theoretical proportions of the components, giving the maximum endoeffect of solution in water.

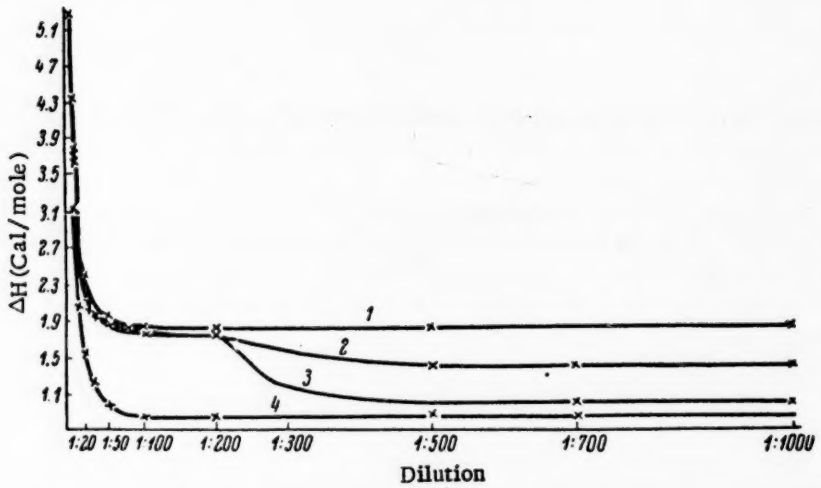
The heats of solution of mercury perchlorate hexahydrate in water were determined for the following dilutions: 1 : 1000, 1 : 500, 1 : 200, 1 : 100, 1 : 50, 1 : 30, 1 : 20, 1 : 10, 1 : 6, and 1 : 4. The average values obtained from 6-7 experiments are given in Table 2.

TABLE 1

Dilution	ΔH (Cal/mole)
1 : 1000	0.85
1 : 700	0 89
1 : 500	0 84
1 : 200	0 87
1 : 100	0 83 ± 0.03
1 : 50	0 98
1 : 30	1 22
1 : 20	1 54
1 : 13	2 07
1 : 10	2 49
1 : 6.7	3,12

TABLE 2

Dilution	ΔH (Cal/mole)
1 : 1000	1.83
1 : 500	1.80
1 : 200	1.83
1 : 100	1.86
1 : 50	1.97 ± 0.04
1 : 30	1.98
1 : 20	2.25
1 : 10	3.08
1 : 6	4.35
1 : 4	5.28



Heats of solution of hexahydrates of the perchlorates of mercury (1), zinc (2), magnesium (3), and cadmium (4) at different dilutions.

The solubility of mercury perchlorate hexahydrate in water at 25° (equal to 7.45 moles of anhydrous perchlorate per 1000 g of water [4]) is exceptionally great. In the microcalorimeter we were able to obtain values for the heats of solution of mercury perchlorate hexahydrate only for a dilution of 1 : 4, which differs considerably from the concentration of a saturated solution.

The values of the heats of solution of the hexahydrates of cadmium and mercury perchlorates given in Tables 1 and 2 are presented in the figure, from which it can be seen that the nature of the curves for the relation of the heat of solution to the dilution for these compounds is similar; the heats of solution of the hexahydrates of cadmium and mercury perchlorates differ only in their absolute values. In this same figure values are given for the heats of solution of the hexahydrates of magnesium and zinc perchlorates, which we have published previously [1, 2]. Thus the values of the heats of solution of the hexahydrates of the perchlorates of the elements of group II of D. I. Mendeleev's periodic system (magnesium, zinc, cadmium, and mercury) are given in the figure. At a dilution of approximately 1 : 30 for the four perchlorates there is a distinct bend in the curve for the heats of solution which divides the whole curve as if into regions of concentrated and dilute solutions. In the region of concentrated solutions the course of the curve for all four perchlorates is the same. Furthermore, the heats of solution of the hexahydrates of three of the perchlorates – magnesium, zinc, and mercury – are practically the same even in absolute value. The heats of solution of cadmium perchlorate hexahydrate for all solutions are lower by approximately the same amount (~0.5 Cal).

As the solution is diluted from 1 : 30, the chemical individuality of the cations is manifested more and more. Attention is attracted by the regularity of the change in the nature of the curves as the solution is diluted in going from magnesium to mercury. On the curve for the heats of solution of magnesium perchlorate hexahydrate there is a sharp decrease in the endoeffect of solution in the region of dilutions from 1 : 200 to 1 : 300 For zinc perchlorate this decrease is considerably less. When the hexahydrates of the perchlorates of cadmium and mercury are dissolved, the heats of solution are unchanged for all the regions of dilution from 1 : 100 to 1 : 1000. When dilute solutions are produced, the heat effect of solution should be considerably influenced by the process of hydrolysis of the salts. According to the data in [5], the perchlorates of the elements mentioned can be arranged with respect to the degree of hydrolysis in the following series: Mg < Cd < Zn < Hg.

SUMMARY

The heats of solution of the hexahydrates of cadmium and mercury perchlorates have been investigated over a wide range of concentrations.

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THE COMPOSITION – PROPERTY DIAGRAM AS A FUNCTION OF THE DEGREE OF CHEMICAL REACTION IN BINARY LIQUID SYSTEMS

I. VISCOSITY DIAGRAMS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3860-3865, December, 1960
Original article submitted January 11, 1960

The rules formulated by N. S. Kurnakov and his followers now permit the satisfactory interpretation of composition–property diagrams for the most prevalent methods of investigation of liquid systems: viscosimetry, conductometry, refractometry, etc. All the investigations in the field of physicochemical analysis of binary liquid systems that have been carried out up to this time, however, have to do exclusively with problems connected with the determination of the composition of the compound formed in the system (for mixtures that react). But for complete characterization of the process, it is important to know not only what compound is formed in the system, but how much of it is produced.

The equations connecting the magnitude of a property in the system with the amount of the compound produced were first derived by N. N. Stepanov [1]. These theoretical developments were conclusively confirmed by experiments.

In recent years calculations of the reaction yield on the basis of data from physicochemical analysis have been thoroughly studied by N. A. Izmailov and his co-workers [2], who have developed a cryoscopic method for the determination of the degree of chemical reaction. The cryoscopic method of calculation of the reaction yield has been developed to a considerable extent in the work of E. E. Cherkashin [3].

All of the methods listed for the calculation of the yield of the reaction between two substances are based on the presence of a third component, the solvent, changes in the properties of which are measured. Thus, the calculations of the degree of chemical reaction have been worked out only for ternary systems and it is not possible to extend them, on principle, to binary systems.* This is why the development of methods for determination of the reaction yield in binary liquid systems is one of the essential problems of physicochemical analysis.

The first stage in such a development must be the establishment of the condition that the composition–property diagram in binary liquid systems in general can be connected with the degree of chemical reaction. The present communication is devoted to the investigation of this question for one of the best worked out methods of physicochemical analysis of binary liquid systems, viscosimetry.

We consider that in the case of the viscosity diagrams of binary systems the degree of chemical reaction must be at least qualitatively connected with the magnitude of the viscosity at the maximum point. One of the

*We are not considering here investigations of the relation of the curvature of the maximum of melting curves to the degree of dissociation of the chemical compound (see, for example, [4]) since in these studies the properties of the liquid phase are not discussed.

TABLE 1

Acetic Acid – Acid Systems at 25°

Second component (acid)	Internal viscosity of second component	Position of viscosity maximum (in mole-% CH_3COOH)	Value of viscosity at maximum point (centipoises)	Relative maximum viscosity	Literature
Perchloric	0.795	67	42.0*	52.8	[8, 9]
Sulfuric	23.17	50	110.16	4.75	[10]
Nitric	0.82**	56	1.874	2.29	[12]
Phosphoric	164.7	30	244.8	1.49	[13]
Chloroacetic	S-shaped isotherm				[14]
Propionic	Isotherm convex toward the composition axis				[15]

*Interpolation from data for 20, 35, and 50°.

**According to data in [11], since there are no data on the viscosity of pure nitric acid in [12].

methods of following the effect of the degree of chemical reaction on the form of the viscosity diagram might be comparison of several systems, where one and the same component reacts with a number of others whose activity with respect to it have been established by independent methods.

Several such series are presented below, the data for which were drawn from literature sources. It must be noted that the possibilities for constructing such series proved to be limited, since all the systems in each series must be compared at one temperature and furthermore we selected only those investigations which seemed to us to be irreproachable with respect to the reliability of the experimental data.

Acetic Acid – Acid Systems

Being a weak acid, acetic acid on reaction with many other acids exhibits a basic function. It is obvious that in binary systems made up of acetic acid and various other acids, the stronger the acid function of the second component the more extensive will be the reaction.

It should be noted that systems made up of two acids are especially convenient for following the connection of the degree of chemical reaction with the magnitude of a property in binary systems, since the strengths of the acids in such solutions usually are considerably different. Thus inorganic acids (perchloric, sulfuric, hydrochloric, etc.) which in aqueous solutions have approximately the same strength differ in strength by 1000 times and more in acetic acid solutions [6].

In Table 1 the main data are given with respect to the viscosity diagrams of acetic acid – acid systems. The position of the viscosity maxima in this and subsequent tables is expressed in mole percent of the first component of the series, in this case acetic acid. The acids are arranged in the order of decreasing acid function. The values of pK for the solutions of these acids in acetic acid were determined by N. A. Izmailov [7]. Thus, in the acetic acid – acid systems we should expect a decrease in the degree of chemical reaction from perchloric to propionic acid.

From the data of Table 1 it can be seen that it is impossible to find an obvious connection between the magnitude of the maximum viscosity in the binary system and the degree of chemical reaction. The reason for this is the effect of the internal viscosity of the second component on the magnitude of the viscosity at the maximum. Actually the viscosity of phosphoric acid, for example, exceeds the viscosity of perchloric acid by more than 200 times. Obviously, therefore, the viscosity at the maximum point in a acetic acid – perchloric acid system is considerably less than in a system with phosphoric acid, although the degree of chemical reaction in the first case must be greater.

TABLE 2

Perchloric Acid–Acid Systems at 50°

Second component (acid)	Internal viscosity of second component	Position of viscosity maximum (in mole-% $HClO_4$)	Value of viscosity at maximum point	Relative maximum viscosity	Literature
Sulfuric*	Isotherm convex toward composition axis			–	[9, 16]
Trichloroacetic	Isotherm convex toward composition axis			–	[17]
Dichloroacetic	S-shaped isotherm			–	[18]
Monochloroacetic	2.15	33	3.55**	1.65	[19]
Acetic	0.742	33	12.68	17.1	[8]
Water	0.549	50	31.97	58.2	[10]

*System investigated at 25°.

**Interpolation from data for 20, 35, and 60°.

TABLE 3

Monochloroacetic Acid–Acid Systems

Second component (acid)	Internal viscosity of second component	Position of viscosity maximum (in mole-% $CH_2ClCOOH$)	Value of viscosity at maximum point	Relative viscosity maximum	Literature
Perchloric	0.55	67	2.44	4.0	[19]
Sulfuric	9.30	30	10.2	1.1	[21]
Nitric	Isotherm convex toward composition axis			–	[21]
Acetic	S-shaped isotherm			–	[14]
Phenol	2.521	10	2.527	1.0	[22]

In order to equalize to some extent the effect of the viscosity of the second component on the magnitude of the maximum, we calculated the values of the relative maximum viscosity, i.e., the ratio of the magnitude of the maximum viscosity in the system to the magnitude of the viscosity of the second component. (Inasmuch as all the systems in each series were compared at the same temperature, the viscosity of the principal component of the series, in the given case of acetic acid, is constant and in the first approximation it can be considered that it does not affect the magnitude of the maximum viscosity in the systems of the series under comparison.) From the data of Table 1 it is seen that the magnitude of the relative maximum viscosity decreases regularly from perchloric to phosphoric acid, in the same direction in which the acid properties of the second components, and consequently the degree of chemical reaction, decrease. In the system with chloroacetic acid the viscosity isotherm has no maximum, but is an S-shaped curve. In the system with propionic acid the viscosity isotherm is convex toward the composition axis, which according to the existing classification of viscosity diagrams indicates the absence of reaction between the components.

Perchloric Acid–Acid Systems

In Table 2 data are given on the viscosity diagrams of perchloric acid–acid systems at 50°. The second components are arranged in the order of their decreasing acid functions. Inasmuch as perchloric acid is one of the strongest acids, all the second components in these systems should be outstanding in relation to it in basicity, as was shown by the investigations of M. I. Usanovich and his co-workers [16-19].

Since the basic functions of the second components of the perchloric acid–acid systems increase from sulfuric acid to water, the degree of chemical reaction in these systems should increase in the same direction. The data of Table 2 agree completely with these ideas. In the first two systems, where the partners of perchloric acid are extremely weak bases–sulfuric and trichloroacetic acids–the viscosity isotherms do not indicate chemical reaction. In the following system the isotherm has an S-shaped form, which indicates a reaction between dichloroacetic and perchloric acids. In the last three systems the viscosity isotherms have a maximum which increases as the degree of chemical reaction increases. The change in relative maximum viscosity is in the same direction.

Monochloroacetic Acid–Acid Systems

In Table 3 data are given on the viscosity diagrams at 60° of systems consisting of monochloroacetic acid and various other acids. The acids are arranged in the table according to decreasing acid functions.

From the data of Table 3 it is seen that the shape of the viscosity isotherm changes regularly with the change in the degree of reaction. In the first two systems, where monochloroacetic acid shows basic functions with respect to its partners, there is a maximum in the isotherms. In the system with nitric acid, there is no reflection of reaction in the viscosity isotherms, since the acid function of nitric acid is more weakly expressed than with perchloric or sulfuric acid. In the next system–with acetic acid–there is an inversion of the function: monochloroacetic acid begins to show its acid properties, while its partner emerges as a base. In conformance with this, reaction is weakly reflected in the S-shaped viscosity isotherm. In the system with phenol, a stronger base than acetic acid, the reaction leads to the appearance of a maximum in the viscosity isotherms.

TABLE 4

Nicotine–Acid Systems

Second component (acid)	Internal viscosity of second component	Position of maximum (in mole-% nicotine)	Value of viscosity at maximum point	Relative viscosity maximum	Literature
Formic	0.6825	31	10.3365	15.12	[23]
Acetic	0.5974	25	7.6179	12.75	[24]
Butyric	0.7283	23.4	5.9923	8.22	[24]
Oleic	7.2624	23.5	11.8200	1.63	[24]
Stearic	8.1362	22.8	13.0609	1.60	[24]

As in the systems with acetic acid, the change in viscosity at the maximum point is not found to have any direct connection with change in the degree of chemical reaction. The relative viscosity maximum, however, changes in accord with the degree of chemical reaction.

We should call attention to the fact that the difference between the magnitudes of the viscosity maximum in the systems with chloroacetic acid is considerably less than in the two preceding series. The reason for this is that monochloroacetic acid, in contrast to acetic and perchloric acids, has no differentiating effect on the strength of the acids dissolved in it [6]. Actually, perchloric and sulfuric acids in acetic acid differ in strength by almost 1000 times (pK is 5.8 and 8.2, respectively); in monochloroacetic acid the difference in strength between these acids is very slight (pK is 1.51 and 1.84, respectively).

TABLE 5

Proportionality of the Magnitudes of the Viscosity Maxima in Two Series of Systems

Second components of the systems	Quotient from division of relative viscosity maxima	
	systems with sulfuric acid	systems with phosphoric acid
$\frac{CH_3COOH}{n\text{-}C_4H_9COOH}$	1.9	1.7
$\frac{CH_3COOH}{iso\text{-}C_4H_9COOH}$	1.6	1.5
$\frac{n\text{-}C_4H_9COOH}{iso\text{-}C_4H_9COOH}$	0.85	0.89

Nicotine-Acid Systems

In Table 4 the essential data are given on the viscosity of nicotine–acid systems, which were studied at 75°. The acids are arranged in order according to the decrease in their acid functions and, consequently, the degree of chemical reaction in the series should decrease from formic acid to stearic.

Although nicotine belongs to the strongly basic substances which sharply increase the strength of acids, the difference in strength of the latter is preserved and possibly even increased because of the low dielectric constant of nicotine (8.94 at 20° [5]).

In the nicotine–acid series, as in the preceding systems, it is impossible to discern any regularity between the magnitude of the viscosity at the maximum point and the degree of chemical reaction. Such a regularity can be followed well, however, if the relative viscosity maximum is used, which decreases as the strength of the acid becomes weaker.

The examples given illustrate the connection between the degree of chemical reaction in binary liquid systems and the appearance of the viscosity diagrams. The number of these examples could be supplemented also by the series acetamide–acids, sulfuric acid–acids, stannic chloride–acids, ethyl acetate–acids, antimony trichloride–acids, etc. These examples, however, cannot illustrate anything new with respect to what has been said.

The statement that the relative viscosity maximum in binary systems where one component is common is a measure of the degree of chemical reaction is not at all quantitative. In other words, if it is found, for example, that the relative viscosity maximum in the system A-B is twice as great as in the system A-C, then this, of course, does not mean that the reaction yield in the first system is twice as great.

However, there are some bases for assuming that the relative viscosity maximum is connected with the magnitude of the reaction yield very directly. If we take two series of systems X–A, X–B. . . and Y–A, Y–B. . . . , then in all the systems of the "X" series the degree of chemical reaction will differ from that for the "Y" series to the same extent (under the condition that X and Y on the one hand, and A and B on the other hand, have the same chemical and classificational characteristics). Table 5 illustrates this for the example of two series of systems: sulfuric acid–lower fatty acids and phosphoric acid–lower fatty acids. The values of the viscosity at 25° were taken from references [13, 25, 26]. It follows from the data presented that the magnitudes of the relative viscosities in the two series are approximately proportional to one another.

SUMMARY

1. It has been shown that in binary liquid systems where there is one common component, the viscosity diagrams are directly related to the degree of chemical reaction.

2. A qualitative change in the degree of chemical reaction is expressed by a change in the relative viscosity maximum.

3. It has been suggested that the relative viscosity maximum is a simple function of the degree of chemical reaction in binary systems.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

ELECTRICAL PROPERTIES OF SYSTEMS FORMED BY TITANIUM TETRACHLORIDE AND ESTERS OF TRICHLOROACETIC ACID

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3866-3869, December, 1960
Original article submitted February 5, 1960

It has been established previously [1-4] that an increase in the electrophilic nature of the acid radical in the molecule of an ester leads to a decrease in the donor properties of the oxygen, as a result of which the stability of the esterates of titanium tetrachloride is considerably decreased.

In the present communication we present the results of measurements of the dielectric permeability of systems formed by titanium tetrachloride with ethyl trichloroacetate, n-butyl trichloroacetate, isobutyl trichloroacetate, and isoamyl trichloroacetate. Furthermore, we present the results of determinations of the dipole moments for some esterates of $TiCl_4 \cdot E$, where E is an ester molecule.

The preparation and purification of the esters and the titanium tetrachloride, and also the methods of measuring the dielectric constant, the density, and the refractive index have been described in previous communications [1, 3, 5]. Here we shall merely note that all measurements were made at 20 ± 0.1°.

In Tables 1-4 the results are given of measurements of the dielectric constants (ε), densities (d), refractive indices (n_D), and also the calculated values of the orientational polarization and the average dipole moments of the systems formed by titanium tetrachloride with the above-mentioned esters of trichloroacetic acid. In the last two columns of the tables are given the deviations of the dielectric constant and the polarization from the additive values.

The magnitudes of the orientation and the dipole moment were calculated by a formula proposed by one of us [6], which connects the dielectric constant of a pure polar liquid with its dipole moment. In the case of binary liquid systems the formula takes the following form:

$$\frac{4}{3}\pi N \cdot \frac{\Sigma u^2}{3kT} = P^{or} = \left[\frac{M_1 \cdot x_1 + M_2 (1 - x_1)}{d}\right] \times \times \left[\frac{(\varepsilon - 1)(\varepsilon + 2)}{9\varepsilon} - \frac{(n^2 - 1)(n^2 + 2)}{9n^2}\right],$$

where $\Sigma\mu$ is the average dipole moment, x_1 is the mole fraction of the first component, M_1 and M_2 are the molecular weights of the components, ε, d, and n are the dielectric constant, the density, and the refractive index of the system as a whole, and P^{or} is the orientational polarization of the solution.

If the components of the system do not change their molecular condition over the entire concentration range, then the magnitudes of the polarization (P^{or}) and the average dipole moments ($\Sigma\mu$) calculated by the above formula will be equal or close to the sum of the polarizations and the moments of the individual components [7, 8]. The presence, however, of a chemical reaction between the components with the formation in the system of complex compounds of a definite composition leads to deviation of the polarization and the average dipole moments

TABLE 1

The System $TiCl_4 - Cl_3CCOOC_2H_5$

Mole % of ester	$t_{20°}$	d_4^{20}	n_D^{20}	p^{or}	$\Sigma\mu$	Δp^{or}	Δs
0.00	2.789	1.7255	1.5856	—	—	—	—
20.00	5.396	1.6530	1.5741	48.45	1.54	23.80	1.48
35.00	6.464	1.6085	1.5530	67.87	1.81	24.74	1.67
50.00	7.840	1.5562	1.5292	91.49	2.10	29.87	2.23
65.00	8.638	1.5061	1.5070	111.87	2.32	31.77	2.30
80.00	8.752	1.4538	1.4828	118.84	2.41	20.25	1.45
100.00	8.428	1.3814	1.4492	123.24	2.48	—	—

TABLE 2

The System $TiCl_4 - n\text{-}Cl_3CCOOC_4H_9$

Mole % of ester	$t_{20°}$	d_4^{20}	n_D^{20}	p^{or}	$\Sigma\mu$	Δp^{or}	Δs
0.00	2.789	1.7255	1.5856	—	—	—	—
20.00	5.283	1.6124	1.5693	49.21	1.54	23.30	1.56
35.00	6.420	1.5366	1.5451	74.05	1.88	28.71	1.98
50.00	7.231	1.4695	1.5214	93.98	2.12	29.20	2.07
65.00	7.593	1.4043	1.4990	110.31	2.31	26.10	1.75
80.00	7.591	1.3449	1.4788	120.34	2.41	16.69	1.26
100.00	7.480	1.2728	1.4508	129.56	2.51	—	—

TABLE 3

The System $TiCl_4 - iso\text{-}Cl_3CCOOC_4H_9$

Mole % of ester	$t_{20°}$	d_4^{20}	n_D^{20}	p^{or}	$\Sigma\mu$	Δp^{or}	Δs
0.00	2.789	1.7255	1.5856	—	—	—	—
20.00	5.467	1.6087	1.5705	52.55	1.60	24.69	1.71
35.00	6.754	1.5325	1.5436	80.29	1.96	31.53	2.25
50.00	7.572	1.4616	1.5242	102.76	2.23	33.10	2.34
65.00	7.930	1.3976	1.5003	118.86	2.40	28.32	1.97
80.00	8.079	1.3372	1.4758	130.29	2.51	18.83	1.39
100.00	7.667	1.2618	1.4470	139.32	2.60	—	—

TABLE 4

The System $TiCl_4 - iso\text{-}Cl_3CCOOC_5H_{11}$

Mole % of ester	$t_{20°}$	d_4^{20}	n_D^{20}	p^{or}	$\Sigma\mu$	Δp^{or}	Δs
0.00	2.789	1.7255	1.5856	—	—	—	—
20.00	5.110	1.5906	1.5664	46.36	1.50	18.47	1.41
35.00	6.461	1.5062	1.5450	78.26	1.94	29.46	2.09
50.00	7.263	1.4312	1.5189	103.16	2.23	33.44	2.21
65.00	7.528	1.3633	1.4986	119.04	2.39	29.40	1.81
80.00	7.634	1.3014	1.4768	132.00	2.53	20.44	1.24
100.00	7.287	1.2300	1.4490	139.45	2.60	—	—

TABLE 5

Dipole Moments of a Number of Complexes of $TiCl_4$

Ester	Dipole moment of esterate $TiCl_4 \cdot E$ (in debye units)
Ethyl trichloroacetate	2.10
n-Butyl trichloroacetate	2.12
Isobutyl trichloroacetate	2.23
Isoamyl trichloroacetate	2.23
Ethyl acetate	4.95
Ethyl propionate	4.88
n-Butyl acetate	4.86
Isoamyl acetate	4.48

from the additive values. The deviation ΔP^{or} from additivity should be proportional to the concentration of the complex compound formed in the system, which makes it possible to judge the composition of the latter compound. It follows from the data in Tables 1-4 that the deviations of the magnitudes of the dielectric constants and the polarizations from additivity in all the systems investigated are considerable; the maximum deviations are in the region of concentrations corresponding to equimolecular ratios of the components.

This circumstance permits the conclusion that in the systems investigated by us the formation of the esterates $TiCl_4 \cdot E$ takes place, with the esterates being highly dissociated at 20° in the liquid phase.

Investigations of a number of physicochemical properties (viscosity, electrical conductivity, heats of mixing) have shown that in systems formed by titanium tetrachloride with esters of acetic acid more stable complexes are obtained in the liquid phase than with the corresponding esters of the chloroacetic acids [1, 3]. As an example, we shall compare the magnitudes of the dipole moments of the complex compounds of titanium tetrachloride with ethyl, propyl, n-butyl, and isoamyl acetates, determined by us from benzene solutions, with the dipole moments of the esterates $TiCl_4 \cdot E$ of trichloroacetic acid. These data are given in Table 5.

From the data of Table 5 it is clear that the introduction of chlorine atoms into the acid radical of the ester leads to a considerable decrease in the magnitude of the dipole moments of the complex compounds formed with titanium tetrachloride.

It must be noted that the dipole moments of the esterates were determined from dilute benzene solutions, where the complex should be subject to a large degree of dissociation. The esterates of $TiCl_4$ with trichloroacetic acid in dilute benzene solutions are almost completely dissociated. All this confirms the conclusion drawn as to the low stability of the complex compounds $TiCl_4 \cdot Cl_3CCOOR$ in the liquid phase and permits the assumption that with an increase in the negative inductive effect of the acid radical, there is a decrease in the dipole moment of the esterates, and consequently in their stability.

This circumstance may be of definite interest in the selection of cocatalysts (activators) for polycondensation of polymerization reactions. For example, the polymerization of styrene under the influence of $TiCl_4$ in toluene and hexane solutions takes place only in the presence of trichloroacetic acid, with which $TiCl_4$ gives a very unstable polar complex that apparently is the active origin of the polymerization [9, 10].

In conclusion, let us note that we have determined the dipole moments of all four of the esters of trichloroacetic acid that were investigated. The moments obtained (Tables 1-4) lie within the limits 2.48-2.60 D, i.e., their magnitude is of the same order as is usually observed for members of a single homologous series. In the literature the dipole moment is given only for ethyl trichloroacetate; it is 2.55 D [11], which agrees closely with our data.

SUMMARY

1. The dielectric constants, refractive indices, and densities of solutions of titanium tetrachloride in ethyl trichloroacetate, n-butyl trichloroacetate, isobutyl trichloroacetate, and isoamyl trichloroacetate have been measured.

2. The magnitudes of the dielectric constant and the orientational polarization show that in solutions of titanium tetrachloride in esters of trichloroacetic acid at 20°, very highly dissociated compounds of equimolecular composition are formed.

3. The dipole moments of ethyl trichloroacetate, n-butyl trichloroacetate, isobutyl trichloroacetate, and isoamyl trichloroacetate have been determined.

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ALKYLATION OF 2- AND 4-CHLOROANISOLES WITH PENTENE-1 IN THE PRESENCE OF THE CATALYST $BF_3 \cdot H_3PO_4$

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3869-3871, December, 1960
Original article submitted February 4, 1960

In the course of the last several years we have investigated the alkylation of halogenated phenols and halogenated anisoles with olefins in the presence of catalysts based on boron fluoride and have shown that this reaction is a very convenient laboratory method for the preparation of interesting, but still not readily available alkylhalogenophenols and their methyl ethers. In the development of these investigations, we report in the present communication the results of the alkylation of 2- and 4-chloroanisoles by pentene-1 in the presence of $BF_3 \cdot H_3PO_4$. It has been found that in contrast to the reaction of 4-chloroanisole with propylene and cyclohexene, and also of 4-bromoanisole with propylene, pseudobutylene, and cyclohexene [1], in this case only mono-sec-amylchloroanisoles are obtained. 2-Chloroanisole is alkylated by pentene-1 approximately 1.5 times more easily than 4-chloroanisole under similar conditions. The optimum conditions, under which 4-sec-amyl-2-chloroanisole was obtained in 86% yield, were molar proportions of 2-chlorophenol, pentene, and catalyst of 3 : 1 : 0.1 and a temperature of 40°. For the preparation of 2-sec-amyl-4-chloroanisole in 54% yield, molar proportions of the reactants and the catalyst of 4 : 1 : 0.2 and a temperature of 40° were required. The yield of alkylation products was not substantially affected by the temperature within limits of 20-60°, proportions of the reactants from 4 : 1 to 2 : 1, nor amounts of catalyst within the limits 0.1-0.3 mole per mole of pentene-1. The best results were obtained when all of the calculated amount of chloroanisole was added at once to the catalyst and the pentene-1 was added slowly to this mixture. When the pentene-1 was mixed with part of the chloroanisole intended for alkylation, the yield of alkylation products was a little less.

EXPERIMENTAL

2- and 4-Chloroanisoles were synthesized by diazotization of 2- and 4- anisidines and cleavage of the diazo derivatives in a manner similar to the synthesis of 4-chlorotoluene [2]. Pentene-1 was prepared by dehydration of normal primary amyl alcohol over Al_2O_3, b.p. 31°, d^{20}_4 0.6410, $n^{20}D$ 1.3712.

The alkylation was carried out by a method previously used [3], adding pentene-1- to a stirred mixture of the chloroanisole and catalyst. In separate experiments with 4-chloroanisole, part of the chloroanisole was mixed with the pentene-1 and added to the catalyst and the rest of the 4-chloroanisole. Addition of the pentene-1 usually was accompanied by the evolution of heat, and therefore in experiments at room temperature the reaction mixture was cooled with cold water. After introduction of the calculated amount of pentene-1, the mixture was stirred for 2 hr more at the temperature of the experiment. At the end of the reaction it had the appearance of a clear light yellow oil, which on treatment with water and sodium carbonate solution became colorless. The reaction products came over in the first distillation of the alkylate almost entirely, within a range of 2-4°. When the alkylate obtained from 2-chloroanisole was distilled, the residue in the flask after the distillation amounted to 0.6-1.2 g, and from the 4-chloroanisole it was about 2-4.6 g. For identification, the alkylation products of all

TABLE 1

Alkylation of 2-Chloroanisole with Pentene-1

Expt. No.	Molar proportions of chloroanisole, pentene-1, and catalyst	Reaction temperature (± 2°)	4-sec-Amyl-2-chloroanisole	
			yield (in %)	boiling limits (pressure in mm)
1	2 : 1 : 0.2	40°	80.9	107—110°(2)
2	3 : 1 : 0.1	40	86.1	108—110 (2)
3	3 : 1 : 0.2	20	81.9	108—110 (2)
4	3 : 1 : 0.2	30	82.4	107—109 (2)
5	3 : 1 : 0.2	40	83.8	107—110 (2)
6	3 : 1 : 0.2	60	85.8	107—110 (2)
7	3 : 1 : 0.3	40	83.3	108—111 (3)
8	4 : 1 : 0.2	40	84.3	108—111 (3)

TABLE 2

Alkylation of 4-Chloroanisole with Pentene-1

Expt. No.	Molar proportions of chloroanisole, pentene-1, and catalyst	Reaction temperature (±2°)	2-sec-Amyl-4-chloroanisole	
			yield (in %)	boiling limits at 2 mm
1	3 : 1 : 0.2	30°	48.9	102—106°
2	3 : 1 : 0.2	40	50.4	102—106
3	3 : 1 : 0.2	60	49.4	104—106
4	3 : 1 : 0.3	40	52.5	102—106
5	4 : 1 : 0.2	40	54.1	103—106
6	4 : 1 : 0.2	40	47.1	101—105
7	4 : 1 : 0.3	40	53.7	102—106

the experiments were combined and again distilled. Their composition and structure were determined by analysis for chlorine by the Carius method, by demethylation to the corresponding phenols, and by conversion of the latter to phenoxyacetic acids. The results of the experiments are given in Tables 1 and 2.

For each experiment 0.1 mole of pentene-1 and the appropriate amounts of chloroanisole and catalyst were used. In Expt. 6 (Table 2) part of the 4-chloroanisole was added to the catalyst, and part was mixed with the pentene-1 and introduced at the time of reaction.

4-sec-Amyl-2-chloroanisole was a colorless, mobile oil with a pleasant odor.

B.p. 107-108° at 3 mm, d^{20}_4 1.0514, $n^{20}D$ 1.5187, MR_D 61.30; calc. 60.53.

Found %: Cl 16.47, 16.38. $C_{12}H_{17}OCl$. Calculated %: Cl 16.67.

4-sec-Amyl-2-chlorophenol was obtained in 72.7% yield by demethylation of 4-sec-amyl-2-chloroanisole with HBr.

B.p. 90-91° at 3 mm, d^{20}_4 1.0798, $n^{20}D$ 1.5240, MR_D 56.30; calc. 55.78.

4-sec-Amyl-2-chlorophenoxyacetic acid was obtained from 4-sec-amyl-2-chlorophenol as white crystals, m.p. 59-60° (from petroleum ether).

2-sec-Amyl-4-anisole was a colorless oil.

B.p. 99° at 2 mm, d^{20}_4 1.0423, $n^{20}D$ 1.5152, MR_D 61.53; calc. 60.53.

Found %: Cl 16.50, 16.44. $C_{12}H_{17}OCl$. Calculated %: Cl 16.67.

2-sec-Amyl-4-chlorophenol was obtained in 64.3% yield by demethylation of 2-sec-amyl-4-chloroanisole. B.p. 110-112° at 3 mm, m.p. 58-59° (from petroleum ether).

2-sec-Amyl-4-chlorophenoxyacetic acid was obtained in 46.2% yield from 2-sec-amyl-4-chlorophenol. M.p. 100-101° (from water).

SUMMARY

The alkylation of 2- and 4-chloroanisoles with pentene-1 in the presence of the catalyst BF_3 H_3PO_4 has been studied.

Conditions have been found under which 4-sec-amyl-2-chloroanisole and 2-sec-amyl-4-chloroanisole are obtained in yields of 86 and 54%, respectively. The alkylchloroanisoles mentioned were demethylated to 4-sec-amyl-3-chlorophenol and 2-sec-amyl-4-chlorophenol, respectively.

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DEMETHYLATION OF ALKYLHALOGENOANISOLES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3872-3873, December, 1960
Original article submitted February 4, 1960

The alkylhalogenoanisoles are still not very readily available, and therefore their chemistry has received almost no study. We have demethylated some alkylhalogenoanisoles. In this we did not have as our goal the study of the rate of demethylation or finding the most favorable conditions for the reaction, but solved only the problem of the synthesis of alkylhalogenophenols. In spite of this, the results obtained permit some interesting conclusions regarding the relationship of the anisole group to hydrobromic and hydriodic acids. First of all we found that all the monoalkyl substituted o- and p-fluoroanisoles and o- and p-chloroanisoles investigated could be demethylated to the corresponding alkylhalogenophenols on prolonged heating with HI or HBr. In this process the cleavage is not quantitative. It is easier to demethylate the 4-alkyl-2-halogenoanisoles, in which the ease of demethylation increases with an increase in the alkyl radical. Of the 14 alkylhalogenoanisoles studied, it was easiest to demethylate 4-sec-amyl-2-fluoroanisole to 4-sec-amyl-2-fluorophenol in 88% yield.

2,6-Dialkyl-4-halogenoanisoles under ordinary conditions are not demethylated by the action of HI or HBr because of the blocking of the methyl group by the two alkyl radicals which are in the two ortho positions. On prolonged heating of 2-cyclohexyl-4-chloroanisole with HI, in addition to demethylation there also occurs the splitting off of a chlorine atom, and as a result 2-cyclohexylphenol is obtained together with the expected 2-cyclohexyl-4-chlorophenol.

EXPERIMENTAL

The alkylhalogenoanisoles necessary for the investigation were prepared by alkylation of the corresponding halogenoanisoles by olefins in the presence of catalysts based on boron fluoride in yields close to quantitative. Demethylation was carried out in the following way. In a 250-ml round-bottomed flask were placed 10-15 g of alkylhalogenoanisole, 100 ml of HI (d 1.7) or 48% HBr, and 50-70 ml of acetic anhydride and the mixture was refluxed at gentle boiling for 45-55 hr. After the reaction mass had cooled, it was diluted with water, neutralized with sodium carbonate, acidified to congo with hydrochloric acid, and extracted with 10% aqueous sodium hydroxide solution. The alkaline solution was acidified with concentrated hydrochloric acid. The phenolic product that separated out upon this treatment was extracted with benzene, the benzene solution was washed with water, dried with sodium sulfate, and distilled. The constants of the starting alkylhalogenoanisoles and also of the demethylation products, the alkylhalogenophenols, and their yields are given in the table.

SUMMARY

Fourteen monoalkyl substituted o- and p-fluoro- and o- and p-chloroanisoles have been demethylated to the corresponding alkylhalogenophenols. The effect of the structure of the alkylhalogenoanisoles on the ease of demethylation has been shown.

Starting alkylhalogenoanisoles						Demethylation products						
Name	boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Name	yield (in %)	boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.
2-Isopropyl-4-fluoroanisole	67° (5)	1.0624	1.4880	45.62	46.33	2-Isopropyl-4-fluorophenole	74.0	75—77° (4)	1.0944	1.5048	41.69	41.48
2-sec-Butyl-4-fluoroanisole	73—74 (3)	1.0234	1.4870	51.18	50.94	2-sec-Butyl-4-fluorophenol	61.7	92 (4)	1.1076	1.5022	44.82	46.19
2-sec-Amyl-4-fluoroanisole	78—79 (3)	1.0050	1.4848	55.95	55.56	2-sec-Amyl-4-fluorophenol	84.7	M.p. 44—45	—	—	—	—
2-Cyclohexyl-4-fluoroanisole	123 (5)	1.0741	1.5142	58.34	57.97	2-Cyclohexyl-4-fluorophenol	64.7	104—105 (2)	1.1231	1.5300	53.38	53.24
4-sec-Amyl-4-fluoroanisole	85 (3)	1.0055	1.4884	56.23	55.56	4-sec-Amyl-2-fluorophenol	87.6	73 (2)	1.0401	1.4974	51.26	50.81
4-Cyclohexyl-2-fluoroanisole	103—104 (2)	1.0652	1.5200	59.41	58.00	4-Cyclohexyl-2-fluorophenol	85.3	M.p. 78	—	—	—	—
2-Isopropyl-4-chloroanisole	72—73 (1)	1.0810	1.5235	52.16	51.29	2-Isopropyl-4-chlorophenol	73.9	126—128 (15)	1.1080	1.5385	48.14	46.55
2-sec-Butyl-4-chloroanisole	84 (2)	1.0583	1.5198	56.99	55.90	2-sec-Butyl-4-chlorophenol	77.5	M.p. 56	—	—	—	—
2-sec-Amyl-4-chloroanisole	99 (2)	1.0423	1.5152	61.53	60.53	2-sec-Amyl-4-chlorophenol***	64.3	M.p. 58—59	—	—	—	—
2-Cyclohexyl-4-chloroanisole	126 (2)	1.1162	1.5460	63.74	62.94	2-Cyclohexyl-4-chlorophenol**	49.1	M.p. 59	—	—	—	—
4-Isopropyl-2-chloroanisole	91—92 (3)	1.0872	1.5245	51.92	51.98	4-Isopropyl-2-chlorophenol	77.8	70—71 (3)	1.1265	1.5336	47.02	46.55
4-sec-Butyl-2-chloroanisole	97—98 (2)	1.0700	1.5220	56.59	55.90	4-sec-Butyl-2-chlorophenol	76.0	82 (3)	1.1061	1.5292	51.45	51.28
4-sec-Amyl-2-chloroanisole	107—108 (3)	1.0514	1.5187	61.30	60.53	4-sec-Amyl-2-chlorophenol***	72.7	90—91 (3)	1.0798	1.5240	56.30	55.78
4-Cyclohexyl-2-chloroanisole	M.p. 56°	—	—	—	—	4-Cyclohexyl-2-chlorophenol	85.4	122—123 (3) M.p. 39	1.1494	1.5544	58.75	58.58

*Literature data: b.p. 120° at 0.3 mm, $n^{25}D$ 1.5470 [1]; b.p. 136-137° at 6 mm, d^{20}_4 1.122, $n^{20}D$ 1.5447 [2].

**Literature data: b.p. 140-142° at 2 mm; m.p. 56° [2]

***Prepared previously [3].

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CYCLOPROPANES AND CYCLOBUTANES

XIV. PHENYLCYCLOPROPANES WITH SUBSTITUENTS IN THE PARA-POSITION OF THE BENZENE RING

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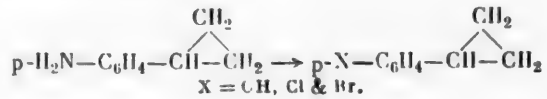
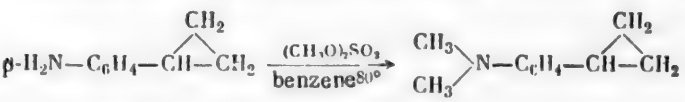
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3874-3876, December, 1960
Original article submitted January 14, 1960

In our previous communications [1-4] devoted to the arylcyclopropanes we noted facts concerning the effect of the aryl radical on the reactivity of the three-membered ring connected to it. Thus, it was found that the tendency to polymerization under the influence of aluminum chloride increased greatly in the order: phenylcyclopropane – p-tolylcyclopropane – p-anisylcyclopropane [2]; the three-membered ring, which breaks easily under the influence of mercuric salts in phenylcyclopropane [3], p-tolylcyclopropane and p-anisylcyclopropane [4], proved to be stable in p-nitrophenylcyclopropane [1]. In order to develop these observations it was necessary to work out a method of synthesizing phenylcyclopropanes containing different substituents in the benzene ring.

As a starting material for the preparation of such compounds, we used p-aminophenylcyclopropane, which, as has been shown in a previous communication [1], is easily obtained by the nitration of phenylcyclopropane and subsequent reduction of the nitro group to an amino group; replacement of the latter in the p-aminophenylcyclopropane by other substituents was accomplished by the diazo reaction. In this way we prepared p-hydroxy-, p-chloro-, and p-bromophenylcyclopropanes.



p-Aminophenylcyclopropane was used also for the synthesis of p-dimethylaminophenylcyclopropane.



Investigation of the Raman spectra of the phenylcyclopropanes prepared showed (by the absence of frequencies in the region 1640-1680 cm^{-1}) that they did not contain contaminating unsaturated compounds; in the region of 1600 cm^{-1}, there were intense frequencies that were related to the aromatic ring; in the region 1200-1260 cm^{-1} we observed lines characteristic of the phenylcyclopropane molecule [5, 6].

The arylcyclopropanes synthesized were characterized by their UV absorption spectra (Figs 1 and 2). The absorption curves had the same character as the absorption curves for p-tolylcyclopropane [5] and p-aminophenylcyclopropane [1]. Characteristic minima were observed in the region 230-250 and 277-278 mμ, and also a characteristic maximum was observed in the region 280-285 mμ.

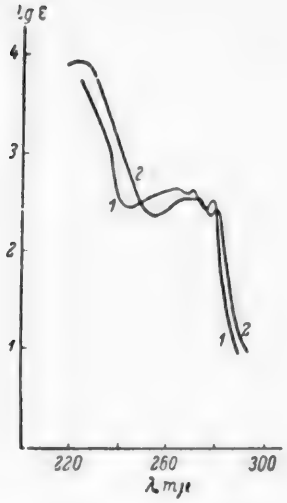


Fig. 1. 1) p-Hydroxyphenylcyclopropane (λ_{min} 240, log ε_{min} 2.37; λ_{max} 273, log ε_{max} 3.35; λ_{min} 277, log ε_{min} 3.24; λ_{max} 279; log ε_{max} 3.36); 2) p-dimethylaminophenylcyclopropane (λ_{min} 233, log ε_{min} 3.68; λ_{max} 250, log ε_{max} 3.84; λ_{min} 277, log ε_{min} 3.21; λ_{max} 283; log ε_{max} 3.23).

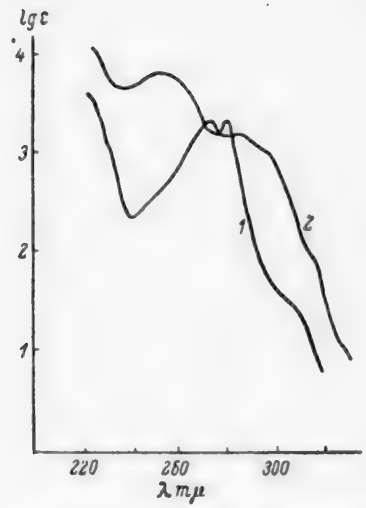


Fig. 2. 1) p-Chlorophenylcyclopropane (λ_{min} 246, log ε_{min} 2.48; λ_{max} 265, log ε_{max} 2.62; λ_{min} 270; log ε_{min} 2.59, λ_{max} 272, log ε_{max} 2.62; λ_{min} 278, log ε_{min} 2.42; λ_{max} 280; log ε_{max} 2.51); 2) p-bromophenylcyclopropane (λ_{max} 223; log ε_{max} 3.91; λ_{min} 252; log ε_{min} 2.35; λ_{max} 266; log ε_{max} 2.52; λ_{min} 270; log ε_{min} 2.51; λ_{max} 273; log ε_{max} 2.56; λ_{min} 278; log ε_{min} 2.36; λ_{max} 280, log ε_{max} 2.43).

EXPERIMENTAL

p-Aminophenylcyclopropane was prepared from phenylcyclopropane by nitration and subsequent reduction of the nitro derivative with powdered iron and hydrochloric acid in calcium chloride solution [1]. Yield 77%.

B.p. 103-104° (9 mm), $n^{20}D$ 1.5810, d^{20}_4 1.0290, MR_D 43.16. $C_9H_{11}NF_3\Delta$. Calculated 42.97.

Literature data [1]: b.p. 100-101° (8 mm), $n^{20}D$ 1.5811, d^{20}_4 1.0291.

p-Hydroxyphenylcyclopropane was prepared from p-aminophenylcyclopropane by the method for preparing phenol from aniline. Yield 50%.

B.p. 98° (7 mm), $n^{20}D$ 1.5618, d^{20}_4 1.0752, MR_D 40.40. $C_9H_{10}OF_3\Delta$. Calculated 40.20.

Found %: C 80.90, 80.79; H 7.63, 7.58. $C_9H_{10}O$. Calculated %: C 80.56; H 7.51.

p-Chlorophenylcyclopropane was prepared from p-aminophenylcyclopropane by the diazo reaction by the same method used for the preparation of p-chlorotoluene from p-toluidine. Yield 59%.

B.p. 76-77° (7 mm), $n^{20}D$ 1.5516, d^{20}_4 1.1122, MR_D 43.79. $C_9H_9ClF_3\Delta$. Calculated 43.54.

Found %: C 71.35, 71.47; H 6.11, 6.22. C_9H_9Cl. Calculated %: C 71.08; H 5.95.

p-Bromophenylcyclopropane was prepared from p-aminophenylcyclopropane by the method for preparing p-bromotoluene from p-toluidine. Yield 30%.

B.p. 101-102° (11 mm), $n^{20}D$ 1.5773, d^{20}_4 1.3902, MR_D 46.93. $C_9H_9BrF_3\Delta$. Calculated 46.44.

Found %: C 55.06, 55.29; H 4.66, 4.71. C_9H_9Br. Calculated %: C 54.84; H 4.58.

p-Dimethylaminophenylcyclopropane. In a 500-ml flask with a reflux condenser was placed a solution of 54 g of p-aminophenylcyclopropane in 200 ml of dry benzene, and then 53 g of dimethyl sulfate was added. When

the violent stage of the reaction ended, the mixture was boiled for 7 hr, the benzene was distilled off, and the residue was heated with 41 g of acetic anhydride for another 4 hr. Sixty ml of 40% sodium hydroxide solution was added to the reaction mixture and the p-dimethylaminophenylcyclopropane that separated out was steam-distilled off, dried with granular potassium hydroxide, and distilled in vacuum. Yield 16 g (25%).

B.p. 97-98° (7 mm), $n^{20}D$ 1.5474, d^{20}_4 0.9757, MR_D 52.40. $C_{11}H_{15}NF_3\Delta$. Calculated 51.85.

Found %: C 81.91, 82.02; H 9.57, 9.52. $C_{11}H_{15}N$. Calculated %: C 81.91; H 9.38.

Raman spectra of the phenylcyclopropanes synthesized were determined in an ISP-51 apparatus with a slit width of 6 cm^{-1}. The intensity of the lines was evaluated visually on a nominal scale where for 10 nominal units we took the intensity of the lines at 1370 cm^{-1} (for p-hydroxyphenylcyclopropane), 1593 cm^{-1} (for p-chlorophenylcyclopropane), 1364 cm^{-1} (for p-bromophenylcyclopropane), and 1204 cm^{-1} (for p-dimethylaminophenylcyclopropane).

p-Hydroxyphenylcyclopropane. 242 (2), 295 (2), 357 (1), 434 (0.5), 494 (0.5), 518 (2), 530 (2), 603 (1), 635 (0.5), 707 (1), 769 (0), 842 (2), 862 (0.5), 892 (0.5), 992 (1), 1037 (15), 1107 (0.5), 1170 (2), 1211 (1), 1258 (12), 1312 (0), 1370 (10), 1427 (2), 1460 (10), 1518 (2), 1571 (1), 1610 (14).

p-Chlorophenylcyclopropane. 127 (4), 201 (4), 276 (1.5), 333 (1), 402 (6), 444 (2.5), 474 (0.5), 518 (2) 546 (0), 567 (2.5), 621 (1), 647 (0.5), 671 (10), 753 (2), 792 (1.5), 822 (1.5), 833 (0.5), 860 (1), 887 (3), 912 (1.5), 965 (1), 996 (0), 1030 (12), 1046 (0), 1092 (1), 1133 (1.5), 1165 (2.5), 1175 (2), 1196 (0), 1219 (9), 1240 (0), 1275 (3), 1362 (6), 1426 (1.5), 1460 (1.5), 1482 (2.5), 1540 (0.5), 1570 (1), 1593 (10).

p-Bromophenylcyclopropane. 192 (4), 248 (1), 303 (3), 340 (2.5), 387 (0), 434 (1.5), 518 (1), 530 (1), 550 (1), 603 (0.5), 635 (0.5), 655 (8), 746 (3), 790 (0.8), 814 (0.5), 859 (0.5), 887 (3), 910 (3), 970 (0.5), 1025 (18), 1080 (1), 1107 (0.5), 1117 (1), 1165 (2.5), 1183 (1.5), 1219 (16), 1270 (2), 1364 (10), 1426 (0.8), 1459 (1), 1473 (1), 1545 (0), 1570 (0.5), 1593 (20).

p-Dimethylaminophenylcyclopropane. 172 (6), 238 (0.2), 257 (0.5), 295 (0.5), 343 (8), 373 (1), 434 (0), 494 (1), 530 (0.5), 560 (1), 574 (2.5), 603 (0), 634 (1), 695 (12), 718 (0), 746 (1), 769 (2), 793 (1), 824 (2), 852 (1), 893-907 (4), 950 (2.5), 978 (0.5), 1020 (2), 1038 (15), 1065 (1.5), 1096 (0.5), 1117 (0.5), 1144 (2), 1165 (8), 1172 (0.5), 1204 (10), 1257 (0), 1296 (2.5), 1315 (2.5), 1357 (5), 1408 (1), 1426 (2.5), 1460 (2), 1473 (1), 1497 (3), 1545 (0.5), 1570 (1), 1601 (40).

SUMMARY

p-Aminophenylcyclopropane was used for the preparation, by the usual reactions, of phenylcyclopropanes not previously described, which were substituted in the para-position—p-hydroxy-, p-chloro-, p-bromo-, and p-dimethylaminophenylcyclopropanes.

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SYNTHESIS OF O-DIPEPTIDYL DERIVATIVES OF ACYLSERINE AND GLYCOLIC ACID

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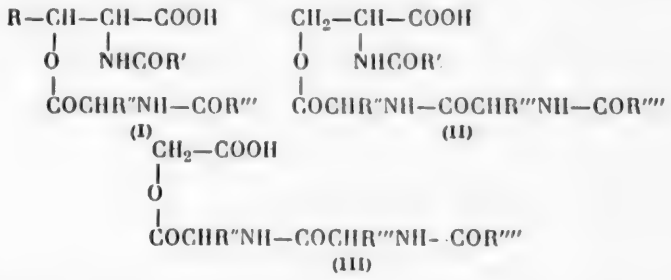
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3877-3883, December, 1960
Original article submitted January 8, 1960

An entire series of O-peptides (I) of serine and threonine have already been synthesized, and the properties of these compounds have proved to be very interesting [1].

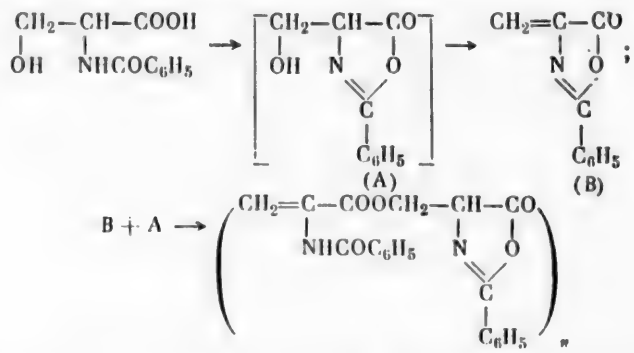


A study of the synthesis and the behavior in enzyme reactions of representatives of a new class of compounds, the O-dipeptidyl-N-acylserines (II), would obviously be of interest. As an approach to the synthesis of such compounds we first studied the synthesis of two corresponding derivatives of glycolic acid (III), O-(benzoylglycylglycyl)- and O-(benzoylglycylphenylalanyl)glycolic acids. The substitution of glycolic acid for serine in the first stage of the investigation was not without basis, since all earlier investigations have shown that serine O-peptides and the corresponding derivatives of glycolic acid have closely similar properties [2]. The O-dipeptidylserines prepared in the present work were O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine and O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine. Several attempts were made to synthesize the corresponding derivatives of benzoylserine, but they were unsuccessful.

The selection of the amino acids for the O-dipeptid[illegible] group was based on earlier observations. Thus, it was found that O-peptides (I) of serine, threonine, and glycolic acid in which the aminoacyl radical was phenylalanyl (R" = $CH_2C_6H_5$), were readily hydrolyzed in the presence of enzyme [2, 3]; under the influence of the enzyme, the phenylalanyl radical migrated to the amino group of other amino acids with the formation of optically active peptides in good yield [2, 4]. Such an observation is in agreement with the distinct specificness of the operation of chymotrypsin when it is the enzyme in enzymatic synthesis [5]; therefore, it was of interest to synthesize and compare first of all O-dipeptidyl derivatives containing phenylalanine directly at the O-peptide bond (the carboxyl group of the phenylalanine takes part in the construction of the O-peptide bond), then compounds in which the phenylalanine is separated from the O-peptide bond (the phenylalanine and the O-peptide bond separated by a glycine), and, finally, compounds which do not contain phenylalanine at all.

At the present time, investigators have at their disposal a rather wide assortment of methods for the synthesis of O-aminoacyl derivatives of hydroxy amino acids (the azlactone, acyl chloride, mixed anhydride, and carbodiimide methods; the latter is suitable for the synthesis of esters of O-peptides); however, the methods suitable for the synthesis of O-dipeptidylserines are practically limited to the single method of mixed anhydrides. Velluz [1] synthesized a series of O-aminoacyl-N-dibenzylserines by this method. However, when we carried out the synthesis of our O-peptidyl derivatives under the conditions indicated by Velluz, we obtained unsatisfactory results. Although O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine was obtained in a yield of 58%, it was contaminated with impurities which could not be removed. Better results were obtained when the reaction was carried out with the reaction mixture cooled to −10 to −12°; in this case, all of the second component was added to the mixed anhydride over a period of 5 min, the reaction mixture was cooled for an additional 30 min, and then allowed to stand at room temperature overnight. O-carbobenzoxyphenylalanylglycyl-N-carbobenzoxyserine was obtained in a yield of 82.8% and O-carbobenzoxyglycylphenylalanyl-N-carbobenzoxyserine was obtained in about 100% yield by this method. Prolonged cooling of the reaction mixture after addition of the second component slows down the reaction with the hydroxyl of the serine and leads to an increase in side reactions.

On the contrary, attempts to synthesize O-carbobenzoxyphenylalanylglycyl-N-benzoylserine and O-carbobenzoxyglycylphenylalanyl-N-benzoylserine were unsuccessful, since, in addition to the main course of the reaction, there were also rapid side reactions, specifically, dehydration and polymerization of the serine derivatives. Such reactions are most typical of benzoylserine, and are less characteristic of carbobenzoxyserine. This is apparently due to the fact that benzoylserine, which is present as the second component, reacts very sluggishly with its own hydroxyl group. On the other hand, a reaction characteristic of benzoyl derivatives of serine does proceed readily; this is a reaction in which the formation of azlactones is accompanied by dehydration. The resulting unsaturated azlactone of benzoylaminoacrylic acid decomposes or enters into a condensation reaction with the formation of more complex compounds which have a neutral character.



The processes described above are possible, obviously, only when a benzoylserine with a free carboxyl group is used as the second component.

In order to confirm our assumptions, a series of experiments was carried out in which the following O-peptides were synthesized: O-benzoylphenylalanyl-N-benzoylserine and its amide, O-dibenzylglycyl-N-benzoylserine, and O-benzoylphenylalanyl-N-tritylserine.

When the reaction was carried out between benzoylserine and benzoylphenylalanine or, as indicated above, between carbobenzoxyphenylalanylglycine and carbobenzoxyglycylphenylalanine a neutral substance was isolated in each case, and the two substances had closely similar chemical compositions. A change in the conditions under which the mixed anhydride with benzoylserine was synthesized had no essential effect on the resulting reaction products. These "neutral" substances gave a positive hydroxamic reaction, did not give a ninhydrin reaction, decolorized an alkaline solution of permanganate, and were easily hydrolyzed by 0.01 N alkali. After hydrolysis with 20% hydrochloric acid, the original amino acids were detected only in traces. It should also be remarked that in spite of the very close attention given to the analyses of the neutral substance obtained in the different reactions, its physical characteristics did not remain constant. The substance did not have a constant melting point, and the higher it was, the lower was the solubility in polar solvents. The reaction apparently does not stop at the stage in which the dimer is formed, and further complication of the molecule takes place.

Similar results were obtained during the synthesis of O-dibenzylglycyl-N-benzoylserine. In those cases in which the second component was the amide of benzoylserine or tritylserine, the formation of O-peptides proceeded normally.

The "negative" role of benzoyl protection is apparently not limited to the cases described; it was also apparent during an investigation of the behavior of benzoyl dipeptides under conditions used for the preparation of mixed anhydrides. Thus, the mixed anhydride formed from benzoylglycylglycine and ethyl chlorocarbonate reacts with ammonia, forming only 10% of the amide; under the same conditions, the amide of benzoylglycylphenylalanine is formed in 12% yield. As would be expected, the mixed anhydride of carbobenzoxyglycylglycine reacts quantitatively with ammonia.

EXPERIMENTAL

O-(Benzoylglycylglycyl)glycolic acid. To a solution of 2.34 g of benzoylglycylglycine and 1.01 g of anhydrous triethylamine in 10 ml of anhydrous methylene chloride, cooled to −10°, was added 1.08 g of ethyl chlorocarbonate, also cooled to −10°. After 5 min, 2.02 g of triethylamine and 1.52 g of glycolic acid were added. The reaction mixture was allowed to stand for 0.5 hr at −10° and then overnight at room temperature. It was then filtered and evaporated. The residual oil was acidified with 10 ml of a 2 N solution of HCl, and then allowed to stand overnight in a refrigerator. The oil did not crystallize completely; the crystallized oil was separated, washed, and repeatedly recrystallized from aqueous alcohol and from ethyl acetate containing petroleum ether. The yield was 0.92 g (31%).

Found %: C 53.65; H 4.83; N 9.87. $C_{13}H_{14}O_6N_2$. Calculated %: C 53.06; H 4.76; N 9.52.

O-(Benzoylglycylphenylalanyl)glycolic acid. To a solution of 2.52 g of benzoylglycylphenylalanine and 0.79 g of anhydrous triethylamine in 20 ml of anhydrous methylene chloride, cooled to −10°, was added 0.845 g of ethyl chlorocarbonate, also cooled to −10°. After 10 min, 1.58 g of triethylamine was added to the reaction mixture, and this was followed by 1.12 g of glycolic acid. The reaction mixture was allowed to stand for 20 min at −10° and then overnight at room temperature; it was then treated as described above. There were obtained 2.1 g of acid (in the form of a foam), which was quickly dissolved in a cold 5% solution of soda, filtered, and acidified with hydrochloric acid. The yield was 1.5 g (50%).

Found %: C 32.59; H 5.57; N 7.22. $C_{20}H_{20}O_6N_2$. Calculated %: C 62.49; H 5.24; N 7.31.

O-(Carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine. To 1.8 g of carbobenzoxyglycylphenylalanine in 4 ml of methylene chloride and 0.7 ml of triethylamine, cooled to −10°, was added 0.5 ml of ethyl chlorocarbonate and, after 10 min, a solution of 1.8 g of carbobenzoxyserine in 4 ml of methylene chloride and 1.05 ml of triethylamine. After 0.5 hr, the reaction mixture was taken from the cooling bath and allowed to stand at room temperature overnight. It was then neutralized with the calculated amount of an 1 N solution of hydrochloric acid and evaporated under vacuum; the residual oil was washed with water. It was converted to a solid foam during azeotropic distillation of the water with benzene. The yield was almost quantitative. The equivalent weight of the resulting material was determined by titration with an 0.01 N solution of base and the ester bond was determined by hydrolysis. For this latter purpose, the sample of the material, after neutralization with 0.01 N base, was refluxed with an excess of the latter for 1.5 hr on a water bath.

Equiv. found: by titration, 582; by saponification, 550. Equiv. calc.: 577.

Found %: C 62.12; H 5.58; N 7.01. $C_{30}H_{31}O_9N_3$. Calculated %: C 62.39; H 5.37; N 7.28.

O-(Carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine. The mixed anhydride was prepared at −12° from 2.38 g of carbobenzoxyphenylalanylglycine, 0.93 ml of anhydrous triethylamine in 5 ml of freshly distilled anhydrous methylene chloride, and 0.49 ml of ethyl chlorocarbonate. After 5 min, the anhydride was reacted with 2.39 g of carbobenzoxyserine and 1.4 ml of anhydrous triethylamine in 5 ml of anhydrous methylene chloride. The reaction mixture was maintained cold for 30 min, and then allowed to stand at room temperature overnight. It was then treated in the usual manner. The yield was 3.2 g (82.8%) of an oil, which was converted to a solid foam during azeotropic distillation of the water with anhydrous benzene. The substance was titrated and saponified as described above.

Equiv. found: 575, 600. Equiv. calc.: 577.

Found %: C 61.98; H 5.79; N 7.05. $C_{30}H_{31}O_9N_3 \cdot {}^1/_2\, H_2O$. Calculated %: C 61.43; H 5.29; N 7.16.

Attempts to synthesize O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine by the method of Velluz. The mixed anhydride was prepared at −10 to −12° from 213 mg of carbobenzoxyphenylalanylglycine, 0.07 ml of anhydrous triethylamine in 1.5 ml of freshly distilled anhydrous methylene chloride, and 0.05 ml of ethyl chlorocarbonate. After 30 min, a cooled solution of 213 mg of carbobenzoxyserine and 0.09 ml of triethylamine in 2 ml of methylene chloride was added. The reaction mixture was maintained at 30° for 9 hr, and allowed to stand at room temperature overnight. The weight of the unpurified material was 180 mg (58%), it was obtained in the form of a solid foam.

Equiv. found: by titration, 462; by saponification, 1478. $C_{30}H_{31}O_9N_3$. Equiv. calc.: 577.

Synthesis of benzoylglycylglycine by the mixed anhydride method. A mixture of 8.5 g of hippuric acid and 4.81 g of triethylamine in 71 ml of anhydrous dioxane was frozen at −13°. The mixture was then removed from the cooling bath, and, after partial thawing of the dioxane, 5.15 g of ethyl chlorocarbonate, previously cooled to −13°, was added dropwise. A cold solution of 4.5 g of glycine in 23.8 ml of a 2 N solution of base and 35.5 ml of water (ratio of dioxane to water, 5 : 4) was added after 10 min. The reaction mixture was maintained at 10° for 1 hr, and was then treated in the usual manner. The yield was 70%; the m.p. was 208°. Literature data: m.p., 206-208° [6]; R_f 0.27 (butanol, saturated with 2 N NH_4OH).

Attempts to synthesize O-(carbobenzoxyphenylalanylglycyl)-N-benzoylserine. The mixed anhydride was prepared from 1.7 g of carbobenzoxyphenylalanylglycine in 3 ml of methylene chloride, 0.7 ml of $(C_2H_5)_3N$, and 0.46 ml of ethyl chlorocarbonate. The anhydride was allowed to stand for 5 min at −7 to −9°, and was then introduced into reaction with a cold solution of benzoylserine (1.6 g) and 1.05 ml of triethylamine in 3 ml of freshly distilled anhydrous methylene chloride. The reaction mixture was allowed to stand in the cold for 0.5 hr and overnight at room temperature. It was then treated in the usual manner. The unpurified material was dried by repeated distillation with anhydrous benzene; this gave a foam which weighed 2.1 g.

Equiv. found: by titration, 746; by saponification, 486. $C_{29}H_{29}O_8N_3$. Equiv. calc.: 547.

The ratio of the equivalent weights indicates the presence of a large amount of neutral material. The product could not be freed from this neutral material by repeated fractional crystallization from aqueous alcohol and a mixture of ethyl acetate and petroleum ether.

Attempts to synthesize O-(carbobenzoxyglycylphenylalanyl)-N-benzoylserine. The mixed anhydride was prepared from 1.78 g of carbobenzoxyglycylphenylalanine in 3 ml of methylene chloride, 0.7 ml of triethylamine, and 0.46 ml of ethyl chlorocarbonate. The mixed anhydride was allowed to stand at −10° for 5 min, and 1.6 g of benzoylserine and 1.05 ml of triethylamine were then added. After 15 min, the reaction mixture was taken from the cooling bath and allowed to stand at room temperature overnight. It was then washed with a 2 N solution of hydrochloric acid and evaporated. The resulting mixture of foam and oil was treated with hot alcohol, and the insoluble material (0.2 g) was removed by filtration. This product was a neutral material which melted at 220°.*

Further recrystallization of that part of the material which dissolved in the alcohol gave a new portion of "neutral" material; O-(carbobenzoxyglycylphenylalanyl)-N-benzoylserine was not isolated.

Synthesis of O-benzoylphenylalanyl-N-benzoylserine by the mixed anhydride method. a) To 1.35 g of benzoylphenylalanine in 8 ml of chloroform was added 0.7 ml of triethylamine and, at −10 to −12°, 0.46 ml of ethyl chlorocarbonate. After 15 min, the reaction mixture was mixed with a cold solution of 1.05 g of benzoylserine in 12 ml of chloroform and 0.7 ml of triethylamine, and this mixture was allowed to stand for 2 days at room temperature. The mixture was then washed with a 2 N solution of hydrochloric acid and evaporated. The residue (1.96 g) was a mixture of (A) benzoylphenylalanine, O-benzoylphenylalanyl-N-benzoylserine and "neutral" material. The "neutral" material was separated from mixture A by repeated extraction with ethyl acetate or a 5% solution of soda in chloroform. This was accompanied by significant hydrolysis of the O-benzoylphenylalanyl-N-benzoylserine. Evaporation of the ethyl acetate solution gave 0.35 g of the "neutral" material in the form of a light yellow, finely crystalline powder.**

*Found, %: C 66.38; H 4.76; N 7.40.

**Found, %: C 65.97; H, 5.04. Equiv.: 1150.

The substance had neither a carboxyl nor an amide group; it gave a positive hydroxamic reaction, and decolorized an alkaline solution of permanganate; it hydrolyzed when heated for 3 hr with an 0.01 N solution of a base. After complete hydrolysis by 20% HCl, traces of phenylalanine were detected by paper chromatography, and there was a series of spots located one after the other with distribution coefficients somewhat lower than the R_f of serine.

When the reaction was carried out in a similar manner, but with an excess of ethyl chlorocarbonate and triethylamine (0.005 mole of benzoylphenylalanine, 0.005 mole of benzoylserine, 0.01 mole of ethyl chlorocarbonate, and 0.02 mole of $(C_2H_5)_3N$], there were obtained 0.33 g of a mixture of benzoylphenylalanine and O-benzoylphenylalanyl-N-benzoylserine and 1.34 g of "neutral" material.

b) Reaction in the cold. Preparation of the mixed anhydride at −70°. To 0.67 g of benzoylphenylalanine in 10 ml of tetrahydrofuran was added 0.38 ml of triethylamine and, at −70°, 0.23 ml of ethyl chlorocarbonate. After 10 min, a solution of 0.52 g of benzoylserine in 10 ml of tetrahydrofuran and 0.38 ml of triethylamine was added to the mixed anhydride solution. The reaction mixture was allowed to stand overnight at −70° to −10° and then for 2 days at room temperature. It was then washed with a 2 N solution of hydrochloric acid and with water. Evaporation of the tetrahydrofuran gave 1.0 g of a mixture consisting of benzoylphenylalanine, O-benzoylphenylalanyl-N-benzoylserine, and a small amount of a "neutral" material. The latter was separated by solution of the mixture in alcohol, neutralization of the solution with a base, and partial evaporation of the alcohol. The precipitated "neutral" material was removed by filtration (0.02 g), and a mixture of benzoylphenylalanine and O-benzoylphenylalanyl-N-benzoylserine was separated from the mother liquor by acidification. Hydrolysis of the mixture of these substances after titration indicated that 30% O-benzoylphenylalanyl-N-benzoylserine was present in it. A small amount of material which was exactly the same as the latter was obtained by interaction of benzoylserine with the mixed anhydride prepared at −70° from benzoylphenylalanine and phosgene by the method of Brenner [1].

Synthesis of O-dibenzylglycyl-N-benzoylserine by the mixed anhydride method. The mixed anhydride was prepared from 0.64 g of dibenzylglycine, 0.38 ml of triethylamine in 7 ml of chloroform, and 0.25 ml of ethyl chlorocarbonate. The mixed anhydride was reacted at −10° with 0.56 g of benzoylserine in 5 ml of chloroform and 0.38 ml of triethylamine. The reaction mixture was held for 4 hr at 20° and 5 hr at 40°, and was then allowed to stand overnight at room temperature. It was then treated in the usual manner. The resulting foam (0.72 g) was only partially soluble in alcohol. The insoluble fraction (0.27 g) was removed by filtration, and reprecipitated with petroleum ether from solution in ethyl acetate. This material was a neutral substance similar to that described above; m.p. 169°.* The substance was reprecipitated five times from ethyl acetate solution with petroleum ether, and the melting point of the resulting material increased to 183°; however, analysis of the material changed very little.

Amide of O-benzoylphenylalanyl-N-benzoylserine. To 1.35 g of benzoylphenylalanine in 10 ml of tetrahydrofuran was added 0.7 ml of triethylamine and, at −80°, 2.2 ml of a toluene solution of phosgene (0.005 mole). After 15 min, 0.52 g of benzoylserine amide in 25 ml of pyridine was added. The cooling bath was removed after an hour, and on the following day the reaction mixture was evaporated under vacuum. Treatment of the residual oil with chloroform precipitated the excess benzoylphenylalanine. A second evaporation yielded 0.95 of an oil, which slowly crystallized under a layer of tetrahydrofuran. After a second crystallization from aqueous alcohol, the material melted at 187-189°.

Found %: C 67.78; H 5.58. $C_{26}H_{25}O_5N_3$. Calculated %: C 67.75; H 5.44.

O-Benzoylphenylalanyl-N-tritylserine. The mixed anhydride was prepared from 0.65 g of benzoylphenylalanine, 0.38 ml of triethylamine in chloroform, and 0.25 ml of ethyl chlorocarbonate. This compound was then reacted with 0.86 g of tritylserine and 0.38 ml of triethylamine in chloroform. The reaction was initially carried out at room temperature. The temperature was then increased to 40° and maintained at that level for 5 hr, after which the reaction mixture was again cooled to room temperature and allowed to stand overnight. The reaction mixture was washed with a 2 N solution of hydrochloric acid and evaporated. The product (1.39 g) was obtained in the form of a solid, slight yellow foam. A weighed portion of the substance was treated to remove the trityl group, and the amount of free amino groups was determined; an excess of base was then added to the

* Found %: C 65.69; H 5.10; N 7.03.

reaction mixture, and the free amino groups were again determined. An estimate of the amount of O-peptide was based on the difference between the two determinations [7]. The value obtained in this manner indicated that 60% O-benzoylphenylalanyl-N-tritylserine was present.

SUMMARY

The following representatives of a new class of O-dipeptidyl-N-acylserines and dipeptide derivatives of glycolic acid were synthesized: O-carbobenzoxyglycylphenylalanyl-N-carbobenzoxyserine, O-carbobenzoxyphenylalanylglycyl-N-carbobenzoxyserine, O-benzoylglycylglycylglycolic acid, and O-benzoylglycylphenylalanylglycolic acid.

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A STUDY OF THE LABILITY OF THE O-PEPTIDE BOND IN O-DIPEPTIDYL DERIVATIVES OF SERINE AND GLYCOLIC ACID

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3883-3890, December, 1960
Original article submitted February 10, 1960

Over the course of the last few years, there has been a sharp increase in interest in the study of O-peptides of β-hydroxy amino acids as labile compounds capable of undergoing decomposition under the influence of enzymes, on the one hand, and, on the other hand, capable of creating new peptide bonds. The discovery of natural compounds containing an O-peptide bond and the strong physiological action of some of them (azaserine) have also promoted intense study of them [1].

$$\begin{array}{l} CH_2-CH-COOH \\ | \quad\quad | \\ O \quad\; NHCOR \\ | \\ COCHR'NH-COCHR''NH-COR''' \end{array}$$

The aim of the present work was to study the properties of the O-peptide bond in more complex derivatives of serine—the O-dipeptidyl-N-acylserines. It was found that an increase in the length of the O-aminoacyl radical had almost no effect on some of the properties of the O-peptides (hydrolysis of the ester bond) and basically changed other properties (synthesis of new peptides). We will consider below alkaline and enzymatic hydrolysis of O-dipeptides, their ammonolysis, and their interaction with esters of amino acids.

The stability of the ester bond in O-dipeptidylserines with respect to bases was studied with O-(carbobenzoxyphenylalanylglycyl)-and O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine, and the results were compared with those obtained in a similar study of O-aminoacyl derivatives of serine (serine O-peptides)—O-benzoylnorleucyl- and O-benzoylvalyl-N-benzoylserine.* The compounds were hydrolyzed at a temperature of 30-32° and a pH of 9, 10, and 10.5 (Fig. 1). As in the case of previously investigated compounds, hydrolysis of the ester bond proceeded very slowly at a pH of 9, and did not exceed 1.5% after 1 hr. The hydrolysis rate increased appreciably with an increase in pH, and at a pH of 10, 12-16% of the substance hydrolyzed in the ensuing hour. The highest hydrolysis rate was observed for the O-dipeptidyl derivative of serine (curve 1), while O-benzoylvalyl-N-benzoylserine hydrolyzed slowest of all (curve 4). This same regularity appeared with an increase in the pH of the solution to 10.5. An increase in the chain length of the O-aminoacyl radical apparently makes the O-peptide bond somewhat less stable toward alkaline hydrolysis.

The difference between O-dipeptidyl and aminoacyl derivatives of serine is considerably more apparent during ammonolysis. It has been shown previously that O-peptides react extremely readily with concentrated ammonia with the formation of amides of acylamino acids in almost quantitative yield [2] (see scheme below).

*The last two compounds were synthesized and investigated by O. M. Shibanova.

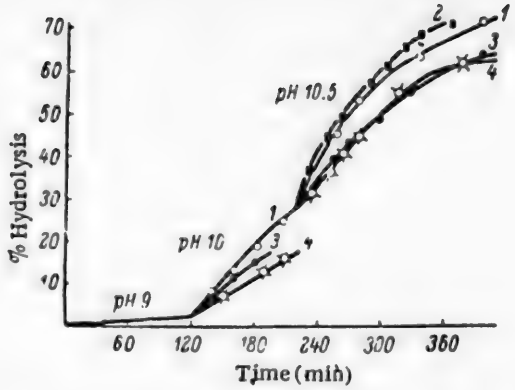


Fig. 1. Hydrolysis rate at various pH values. 1) O-(Carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine, 2) O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine, 3) O-(benzoylnorleucyl)-N-benzoylserine, 4) O-(benzoylvalyl)-N-benzoylserine.

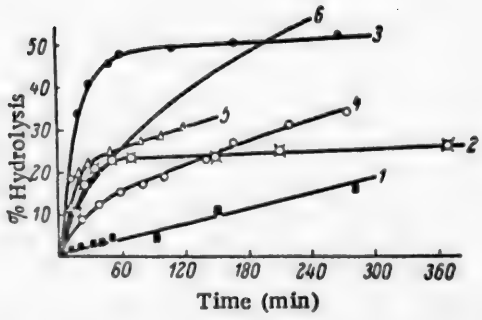
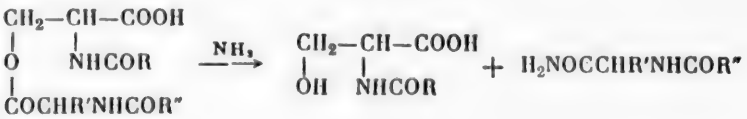


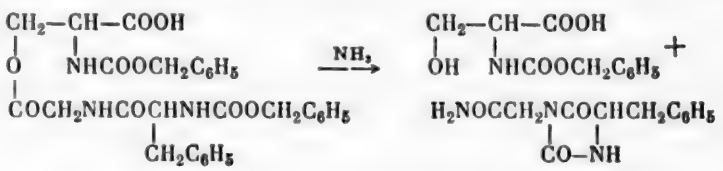
Fig. 2. Comparison of the rates of hydrolysis of different compounds. 1) O-(benzoylglycylglycyl)glycolic acid, 2) O-(benzoylglycylphenylalanyl)glycolic acid, 3) O-(benzoylglycyl)glycolic acid, 4) O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine, 5) O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine, 6) O-(benzoylphenylalanyl)-N-benzoylserine.

Dipeptidyl derivatives of serine and glycolic acid are significantly less readily converted to the corresponding amides. Although the treatment of O-(benzoylglycylglycyl)glycolic acid with 28 % ammonia at room temperature gave a 70% yield of benzoylglycylglycine amide, O-(benzoylglycylphenylalanyl)glycolic acid was converted to the amide under even more vigorous con-

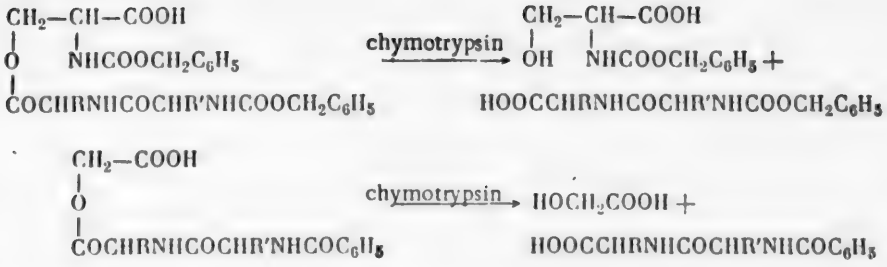


ditions (30-40°) with a yield of only 40%. However, after a 12-hr treatment, carbobenzoxyphenylalanylglycine was obtained in 73% yield from O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine. Thus, hydrolysis of the O-peptide bond takes place more readily than does ammonolysis.

The interaction of this same O-dipeptide with a solution of ammonia in chloroform yielded a compound which, although it possessed neutral characteristics, was not an amide. It was obtained in the form of an oil which, upon very long standing, partially converted to a crystalline material with an m.p. of 216-218°; this value differs from the melting point of carbobenzoxyphenylalanylglycine amide. It may be supposed that the well-known tendency of the ethyl ester of carbobenzoxyphenylalanylglycine to be converted to a hydantoin under the influence of a methanol solution of ammonia [3] takes place in the present case with closure of a ring:

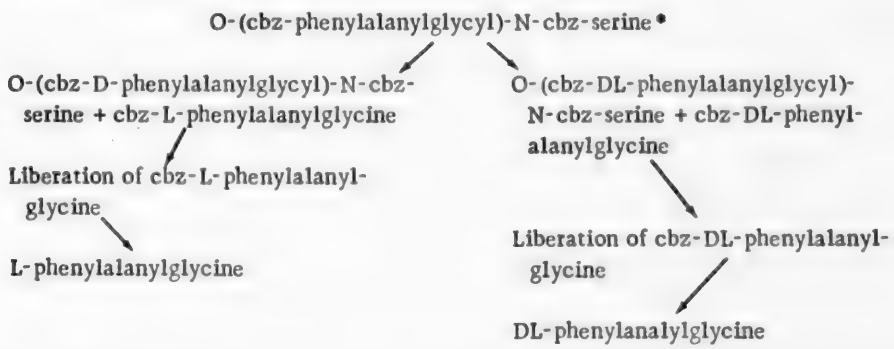


Hydrolysis of the ester bond by chymotrypsin was studied with two O-dipeptidyl derivatives of serine and two dipeptidyl derivatives of glycolic acid. Specifically, the following compounds were used: O-(carbobenzoxyphenylalanylglycyl)- and O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine and O-(benzoylglycylglycyl)- and O-(benzoylglycylphenylalanyl)glycolic acid.



The results obtained are shown in Fig. 2. For purposes of comparison, the courses of hydrolysis of O-benzoylphenylalanyl-N-benzoylserine [4] and O-benzoylglycylglycolic acid are also presented in the same figure. All of the compounds enumerated were hydrolyzed by the enzyme, but the rates of hydrolysis of the different peptides differed considerably among themselves. The dipeptidyl derivatives of both serine and glycolic acid hydrolyzed more poorly, on the whole, than did the O-aminoacyl derivatives. It is interesting that during the first 30 to 60 min, their hydrolysis rates were very high, and, in this regard, there was no distinction between the O-dipeptides and the O-peptides. However, subsequent to this period, there was a sharp break in the hydrolysis rate curve, and hydrolysis almost stopped at this point. Hydrolysis of O-(carbobenzoxyphenylalanylglycyl)- and O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine and O-(benzoylglycylphenylalanyl)-glycolic acid conforms to curves of this type (with a break). A comparison of the rates of hydrolysis of the two O-dipeptidyl derivatives of serine shows that hydrolysis proceeds at a greater rate when the phenylalanyl radical is attached directly at the hydrolyzing bond—O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine was more readily hydrolyzed by the enzyme than was O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine. Hydrolysis of these peptides does not take place under the same conditions, but in the absence of an enzyme.

Enzymatic hydrolysis of O-peptides of hydroxy amino acids and the corresponding derivatives of glycolic acid takes place asymmetrically; under the action of the enzyme, cleavage of only that half of the O-peptide, which contains the L-form of the O-acylamino acid takes place. It appeared possible, in the present work, to determine the nature of the participation of chymotrypsin-promoted hydrolytic reactions of the asymmetric atom of an amino acid not directly attached at the hydrolyzing ester bond. For this purpose, an enzymatic hydrolysis of O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine was carried out; in this compound, the ester bond formed by the glycine is removed from the acid containing an asymmetric atom. Two variants of the cleavage occurring during hydrolysis may be proposed:



In the first variant, cleavage proceeds asymmetrically, and carbobenzoxy-L-phenylalanylglycine is formed; in the second variant, the asymmetric center of the phenylalanine is not affected, and carbobenzoxy-DL-phenylalanylglycine is formed.

For comparison, the enzymatic hydrolysis of O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine was carried out; the succession of amino acid and dipeptide residue is reversed in this compound. In this case, it would be expected that the optically active peptide would be obtained.

*cbz—carbobenzoxy.—Publisher's note.

O-(cbz-glycylphenylalanyl)-N-cbz-serine

↓

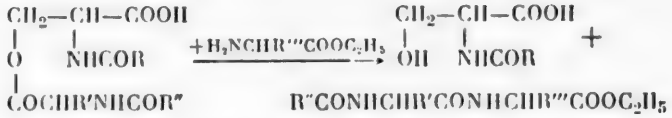
O-(cbz-glycyl-D-phenylalanyl)-N-cbz-serine +
+ (cbz-glycyl-L-phenylalanyl)-N-cbz-serine

↓

Liberation of cbz-glycyl-L-phenylalanylserine

The O-dipeptidyl derivatives of serine were incubated with chymotrypsin for 4 hr at 20° and a pH of 8.2. The reaction mixture was made acid, and the precipitated oil was freed of carbobenzoxyserine by repeated washing with water. This oil was a mixture of O-dipeptide and the corresponding peptide which had been split off. As would be expected, in the case of the hydrolysis of O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine, the mixture was appreciably dextrorotatory. We were unable to detect any optical activity in the case of the hydrolysis of O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine. Then, on the basis of the ability of O-peptides to undergo conversion to a substance having neutral characteristics under the action of ammonia, it appeared possible to isolate from the first mixture the carbobenzoxy dipeptides and to measure their specific rotation. The specific rotation of carbobenzoxyglycylphenylalanine was appreciably higher, while that of carbobenzoxyphenylalanylglycine remained zero. The latter compound was converted by hydrogenation into phenylalanylglycine, which was also optically inactive. Thus, it has been shown that the asymmetric character of enzymatic hydrolysis of O-dipeptidylserines is determined only by the amino acid attached directly at the O-peptide bond.

A process which is being widely studied at the present time is the transfer, under the influence of chymotrypsin, of an O-aminoacyl radical of O-peptides of serine, threonine, and glycolic acid to an amino group of esters of amino acids or dipeptides with the formation of new di- and tripeptides [5].



It was interesting to study the possibility of the migration of an O-dipeptidyl group to the amino group of an amino acid ester. Toward this end, the following pairs of compounds were incubated for a period of 3 to 4 hr at a pH of 8.0 and a temperature of 20°: O-(benzoylglycylglycyl)glycolic acid and the ethyl ester of leucine, O-(benzoylglycylphenylalanyl)glycolic acid and the ethyl ester of valine, O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine and the ethyl ester of alanine, and O-(carbobenzoxyglycylphenylalanyl)-N-carbobenzoxyserine and the ethyl ester of leucine.

A characteristic peculiarity of the process of forming a new peptide is usually the rapid precipitation of the resulting ester of the N-peptide. However, in all of the cases enumerated above, the incubated solutions remained completely transparent. Therefore, the initial reactants were removed from the reaction mixture, and the remaining material was hydrolyzed with a 20% solution of hydrochloric acid; the hydrolysis products were chromatographed in various systems. The chromatograms contained spots for all of the amino acids; however, their number was extremely small, and spot intensity was the same for the experimental and control solutions.

By way of example, the experiment with O-(benzoylglycylglycyl)glycolic acid is described in the Experimental section of this paper.

Thus, an increase in the chain length of the aminoacyl radical exerts a basic effect on the behavior of the ester bond in O-peptides of β-hydroxy amino acids. It somewhat more readily undergoes alkaline hydrolysis, but it reacts more difficultly with ammonia. Of particular interest is the behavior of the ester bond of O-dipeptidylserines toward chymotrypsin. Chymotrypsin hydrolyzes this bond, but it does not promote synthesis reactions with amino acid esters even when phenylalanine is present in the dipeptide residue.

EXPERIMENTAL

Alkaline hydrolysis. a) The O-dipeptidyl derivative of serine was dissolved in 3 ml of acetone, and an equimolar amount of a 0.1 N solution of the base was added, followed by 4 ml of water. More of the 0.1 N alkaline solution was then added until the desired pH was reached. The reaction mixture was placed in a thermostatted

bath at a temperature of 30-32°, and, after a specific interval of time, the pH was brought to its original value by titration with the 0.1 N alkaline solution. The titration was carried out potentiometrically. The results of these hydrolysis experiments are presented in Fig. 1 (curves 1 and 2).

b) The O-aminoacyl derivative of serine was dissolved in 20 ml of 50% alcohol, and 0.1 N base was added to this solution until the predetermined pH value was reached. Measurements were then made as described for the preceding experiments. The results are presented in Fig. 1 as curves 3 and 4.

O-Benzoylnorleucyl-N-benzoylserine was prepared by the acid chloride method from benzoylserine and benzoylnorleucyl chloride; m.p. 180.5° after recrystallization from 50% alcohol.

Found %: C 64.93; H 6.17; N 6.09. $C_{23}H_{26}O_6N_2$. Calculated %: C 64.80; H 6.10; N 6.57.

The methyl amide of O-benzoylnorleucyl-N-benzoylserine was prepared from the methyl amide of benzoylserine and benzoylnorleucyl chloride; m.p. 123° (from 50% alcohol).

Found %: C 65.60; H 6.79; N 9.54. $C_{24}H_{29}O_5N_3$. Calculated %: C 65.80; H 6.60; N 9.56.

The O-benzoylvalyl-N-benzoylserine was prepared from benzoylserine and benzoylvalyl chloride; m.p. 170-171° after recrystallization from aqueous alcohol.

Found %: C 64.04; H 5.86; N 6.79. $C_{22}H_{24}O_6N_2$. Calculated %: C 64.07; H 5.87; N 6.79.

The methylamide of O-benzoylvalyl-N-benzoylserine was prepared from the methylamide of benzoylserine and benzoylvalyl chloride; two diastereoisomers were separated. The first had an m.p. of 167° (this substance was soluble in acetone, chloroform, and dichloroethane), and the second had an m.p. of 205° (this substance was insoluble in acetone, chloroform, and dichloroethane).

Analysis of the substance with an m.p. of 167°.

Found %: C 64.92; H 6.58; N 9.70. $C_{23}H_{27}O_5N_3$. Calculated %: C 64.94; H 6.35; N 9.88.

Analysis of the substance with an m.p. of 205°.

Found %: N 9.87. $C_{23}H_{27}O_5N_3$. Calculated %: N 9.88.

Ammonolysis experiments. a) A sample of O-(benzoylglycylglycyl)glycolic acid weighing 58.2 mg was treated with 1 ml of a 28% solution of ammonia. A precipitate began to form after 2 min, and after 1 hr, the precipitate was separated by filtration, washed with 1 ml of water, and dried. The yield of benzoylglycylglycine amide was 38 mg (73%); m.p. 204°; the literature gives a value of 202° for the m.p. [6].

b) A sample of O-(benzoylglycylphenylalanyl)glycolic acid weighing 109.2 mg was treated with 1 ml of 28% ammonia silution. A slight turbidity was noted after 10 min. The reaction mixture was heated to 30-40° over a period of 20 min, and was then allowed to stand overnight at room temperature. The resulting precipitate was separated by filtration, washed with 1 ml of water, and dried. The yield of benzoylglycylphenylalanine amide was 34 mg (40%), m.p. 179-180°.

Found %: C 66.28; H 5.96. $C_{18}H_{19}O_3N_3$. Calculated %: C 66.44; H 5.88.

c) A sample of O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxy serine weighing 215 mg was dissolved in 5 ml of 28% ammonia solution. Solution occurred immediately, and the solution appeared slightly turbid. The reaction mixture was allowed to stand overnight at 0-5°, and was then evaporated to 2/3 its volume and filtered. The filtrate was acidified, and 88 mg (73.5%) of carbobenzoxyphenylalanylglycine was obtained.

Enzymatic hydrolysis. a) To 0.5 mmole of O-(dipeptidyl)glycolic acid dissolved in 3 ml of hot alcohol and 1 ml of water were added, after cooling, 0.5 ml of a 1 N solution of NaOH and 2 ml of phosphate buffer (8.0 pH). The pH of the reaction mixture was brought to 7.9-8.1 by potentiometric titration, and the reaction mixture was then allowed to stand at 20° in a thermostatted bath. The pH of the solution did not change over a period of 2 hr, and 5-7 mg of the enzyme was then added to the reaction mixture. After a specific time, the pH of the solution was measured potentiometrically, and was returned to its original value by the addition of 0.1 N base. The results of the measurements are presented in Fig. 2 (curves 1 and 2). For comparison, the hydrolysis of O-benzoylglycylglycolic acid was studied under analogous conditions (curve 3).

b) A weighed sample of the O-dipeptidylserine was dissolved in 3 ml of acetone, and to the solution were added an equimolar amount of the 1 N base solution, 1 ml of phosphate buffer (pH 8.1), 4 ml of water, and 5 mg of the enzyme. The course of the hydrolysis was followed in a manner similar to that described above. The results are presented in Fig. 2 (curves 4 and 5).

Separation of the products from the enzymatic hydrolysis of O-dipeptidylserines. a) Hydrolysis of the ester bond of O-(carbobenzoxyphenylalanylglycyl)-N-carbobenzoxyserine by chymotrypsin. A 1.4994-g sample of the O-peptide was hydrolyzed with 10 mg of chymotrypsin under the conditions described above. After 4 hr, the acetone was evaporated, and the reaction mixture was acidified with a 2 N solution of hydrochloric acid to precipitate an oil (A), which was repeatedly ground with water. The weight of oil (A) was 1.0531 g; $[\alpha] = 0$ (1.0531 g in 16 ml of alcohol).

b) Separation of carbobenzoxyphenylalanylglycine from mixture A. An 0.0837 g portion of oil A was dissolved in 10 ml of chloroform saturated with ammonia and allowed to stand for 3 days at −5°. The chloroform solution was partially evaporated, and the residue was repeatedly extracted with water. The aqueous extract was acidified, and 0.3345 g of carbobenzoxyphenylalanylglycine was obtained; m.p. 144-146°; $[\alpha] = 0$ (0.2018 g in 3 ml of 98% acetic acid).

c) Conversion of carbobenzoxyphenylalanylglycine to phenylalanylglycine. An 0.0746 g sample of carbobenzoxyphenylalanylglycine was hydrogenated in the usual manner over Pd/C. The hydrogenation was considered finished when 98.6% of the calculated amount of CO_2 had been evolved. The yield of phenylalanylglycine was 0.4413 g (94%); $[\alpha] = 0$ (40 mg in 1 ml of water).

d) Hydrolysis of the ester bond of O-(carbobenzoxyglycylphenylalanyl-N-carbobenzoxyserine by chymotrypsin. The hydrolysis was carried out in a manner analogous to that described above. From 1.4946 g of the material was obtained 1.1835 g of an oil (mixture B); $[\alpha]^{20}D + 3.5°$ (0.8150 g in 18 ml of alcohol). Part of the mixture, 0.4391 g, was treated with a saturated solution of ammonia in chloroform, and 0.1656 g of carbobenzoxyglycylphenylalanine was obtained; m.p. 125-127°, $[\alpha]^{20}D + 10.8°$ (0.0856 g in 15 ml of alcohol).

Literature data: for carbobenzoxyglycyl-L-phenylalanine, m.p. 122-124°; $[\alpha]^{26}D + 38.5°$ (0.05 g in 2 ml of alcohol) [3].

Interaction of O-(benzoylglycylglycyl)glycolic acid with the ethyl ester of leucine in the presence of chymotrypsin. a) A solution of 458 mg of O-(benzoylglycylglycyl)glycolic acid in 12 ml of hot alcohol was cooled and then titrated with a base, and the alcohol was then distilled under vacuum. To the residue were added 1.479 g of the ethyl ester of leucyl chloride in 7.56 ml of 1 N base and 2 ml of phosphate buffer (pH 8.0). The pH of the reaction mixture was then brought to 8.08, 5-7 mg of the enzyme was added, and the mixture was allowed to stand in a thermostatted bath at 20°. A slight turbidity appeared in the solution after 3 hr. Two-thirds of the solution was extracted with ethyl acetate, and the extract was washed with a 2 N solution of hydrochloric acid, a 10% solution of soda, and water. The ethyl acetate was distilled under vacuum, and the residual oil was hydrolyzed for 7 hr with a 20% solution of hydrochloric acid. The solution was evaporated to dryness under vacuum, and the residue was dissolved in 0.5 ml of acetic acid. The hydrosylate was chromatographed in the system 1-butanol−water−acetic acid (4 : 5 : 1), and only insignificant amounts of glycine and leucine were found. To the remaining third of the solution were added a solution of 100 mg of O-(benzoylphenylalanyl)glycolic acid in alcohol and an equivalent amount of base. Precipitation began after 10 min. This material was benzoyl-L-phenylalanyl-L-leucine, the amino acid composition of which was determined by means of paper chromatography.

b) A 151-mg sample of O-(benzoylglycylglycyl)glycolic acid was treated with 500 mg of the ethyl ester of leucyl chloride in the manner described above, but in the absence of enzyme; only insignificant amounts of glycine and leucine were detected by chromatography.

SUMMARY

1. A study was made of the behavior of the ester bond in O-dipeptidyl derivatives of serine and glycolic acid during alkaline and enzymatic hydrolysis and during ammonolysis.

2. It was shown that, in contrast to the O-aminoacyl derivatives of serine and glycolic acid, the O-dipeptidyl derivatives are more easily hydrolyzed by bases, react more difficultly with ammonia, are hydrolyzed by chymotrypsin, and do not enter into reaction with esters of amino acids under the influence of chymotrypsin.

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INVESTIGATIONS IN THE FIELD OF CONJUGATED SYSTEMS

CXXVI. THE ADDITION OF LITHIUM ALKYLS TO VINYLACETYLENIC ALCOHOLS*

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3890-3894, December, 1960
Original article submitted January 21, 1960

Vinylalkylacetylenes readily add lithium alkyls with the formation, after treatment of the addition product with water, of disubstituted allenic hydrocarbons [1]. Divinylacetylene and its homologs behave in a similar manner with respect to addition of lithium alkyls. Vinylallenes are obtained in this case. The addition of the alkyl radical to unsymmetrical dienes proceeds predominantly on the side of the unsubstituted vinyl group [2].

It therefore seemed of interest to investigate the manner of addition of lithium alkyls to derivatives of vinylalkylacetylenes, in particular, to vinylacetylenic alcohols.

Secondary and tertiary vinylacetylenic alcohols—methyl- and dimethylvinylacetylenylcarbinols—were selected as objects of investigation in the present work. The reaction mixture was carried out in ether with cooling of the mixture during the reaction, i.e., under the conditions previously used during the study of the addition of lithium alkyls to hydrocarbons. Demetallation was carried out with water.

In all cases, the reaction proceeded without any complication and with the almost exclusive formation of allenic alcohols in accordance with the scheme (for a secondary alcohol):

$$R-CHOH-C\equiv C-CH=CH_2 \xrightarrow{R'-Li} R-CHOH-CLi=C=CH-CH_2-R' \xrightarrow{H_2O} \longrightarrow R-CHOH-CH=C=CH-CH_2-R'$$

The structure of the carbon skeleton in the product alcohols was proved by hydrogenation of the alcohols to the corresponding saturated compounds and alternate synthesis of the latter.

Hydrogenation of the alcohol obtained from the product of the addition of butyllithium to methylvinylacetylenylcarbinol (1-hexen-3-yn-5-ol) gave 2-decanol; the properties and infrared spectrum of this product were closely similar to those of 2-decanol prepared by the action of octylmagnesium bromide on acetaldehyde. Oxidation of these two samples of 2-decanol gave the same methyl octyl ketone (2-decanone).

Hydrogenation of the tertiary alcohol obtained from the addition of butyllithium to dimethylvinylacetylenylcarbinol gave dimethyloctylcarbinol (2-methyl-2-decanol), which was almost identical in physical properties and infrared spectrum to 2-methyl-2-decanol prepared by the action of octylmagnesium bromide on acetone.

It has thus been established that in both of these cases the radical adds to the terminal carbon atom of the conjugated system.

The question of the disposition and nature of the multiple bonds was unequivocally resolved on the basis of an investigation of the infrared spectra of the unsaturated alcohols. These spectra (Fig. 1) contained a very

*Enyne compounds. XLVI.

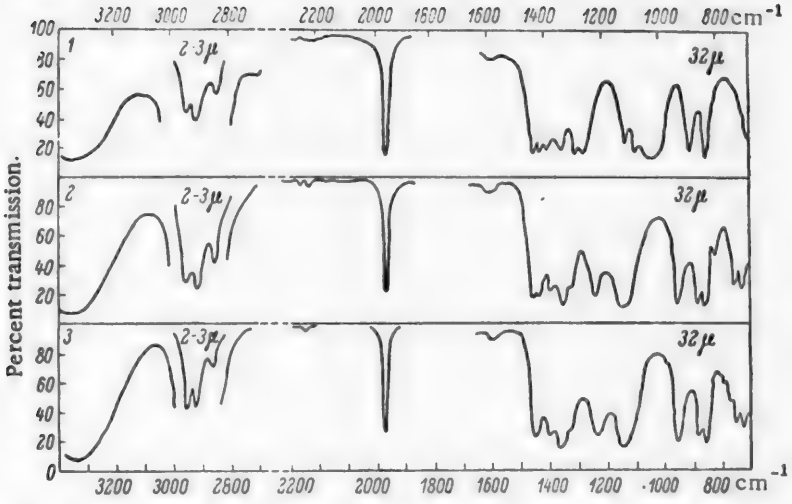

Fig. 1. Infrared transmission spectra (film thickness, 32 μ). 1) 3,4-Decadien-2-ol, 2) 2-methyl-3,4-decadien-2-ol, 3) 3,4-nonadien-2-ol.

strong band at 1970 cm^{-1} as well as a band at 875 cm^{-1}; these bands are characteristic of disubstituted allenes. The corresponding frequencies for acetylenic (about 2250 cm^{-1}) and 1,3-diene (about 1600 cm^{-1}) groups were very weak (Fig. 1, curves 1-3).

All of these data indicate that, as in the case of hydrocarbons (vinylalkylacetylenes), the addition of lithium alkyls to vinylacetylenic alcohols proceeds with the almost exclusive formation of allenic alcohols; however, acetylenic and 1,3-dienic alcohols were present as slight impurities.

The acetylenic alcohols are most probably products of allene–acetylene isomerization of the primary addition products at the instant of addition or during the subsequent treatment of the addition products with water. A similar assumption may be made relative to the origin of the 1,3-dienic alcohols; they are probably formed as the result of an allene–1,3-diene rearrangement, and not as the result of the addition of the lithium alkyl at the triple bond, since, if the latter were the case, 1,3-dienes with a vinyl group would be formed, and the bands of the vinyl group were not present in the spectra.

It is also possible that the acetylenic alcohols are formed during the water treatment of lithium alkyl addition products of the following structure:

$$R—CHOH—C\equiv C—CHLi—CH_2—R'.$$

Thus, the previously established rule regarding the manner of addition of lithium alkyls to vinylalkylacetylenes can now be extended to alcohols in which the structure of the enyne system is the same as in the hydrocarbons.

EXPERIMENTAL

The original methylvinylacetylenylcarbinol (1-hexen-3-yn-5-ol) was prepared by the action of vinylacetylenylmagnesium bromide on acetaldehyde [3]. The dimethylvinylacetylenylcarbinol (5-methyl-1-hexen-3-yn-5-ol) was a commercial product. It was distilled prior to the experiments.

The method by which the addition of lithium alkyls was carried out has been described previously [1]. In the present work, the ether solutions of lithium alkyls were prepared from 6 g of lithium and the corresponding amounts of alkyl chlorides.

Addition of butyllithium to methylvinylacetylenylcarbinol. The reaction of 12 g of methylvinylacetylenylcarbinol with the ether solution of butyllithium and subsequent treatment of the reaction mixture with water gave 14.5 g of a substance with the constants given below and 3 g of higher-boiling residue which formed a tar during the distillation.

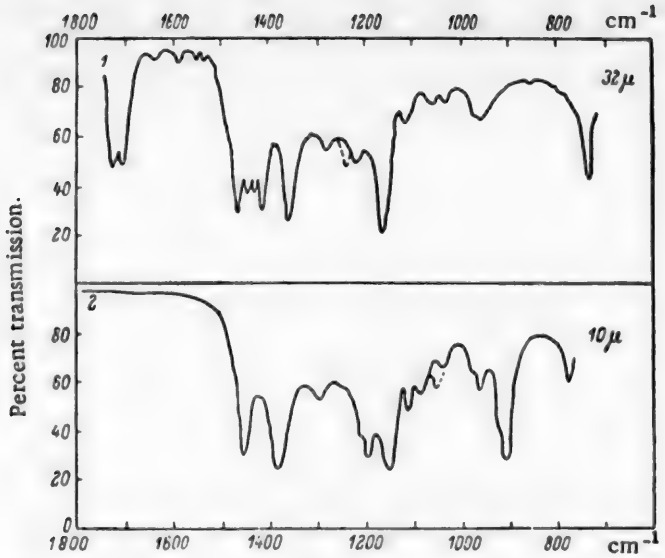

Fig. 2. Infrared transmission spectra. 1) 2-Decanone, 2) 2-methyl-2-decanol (differing frequencies for known samples are shown as broken lines).

3,4-Decadien -2-ol. B.p. 97-98° (10 mm), 111-112° (20 mm), d^{20}_4 0.8563, $n^{20}D$ 1.4690, MR 50.16; calc. 48.97.

Found %: C 78.07, 77.83; H 11.97, 11.85. $C_{10}H_{18}O$. Calculated %: C 77.86; H 11.76.

I. r.-spectrum: 730 s, 840 w, 875 s, 925 s, 1060 s, 1079 s, 1116 s, 1146 s, 1240 av, 1297 s, 1318 s, 1373 s, 1429 s, 1450 s, 1464 s, 1603 vw, 1972 s, 2701 w, 2862 s, 2932 s, 2962 s, 3400-3500 vs cm^{-1}.

During exhaustive hydrogenation of 3.67 g of the substance over colloidal palladium, 481 ml H_2 (17.5°, 771 mm) was absorbed; this is about 84% of the calculated amount. There was obtained 3.0 g of methyloctylcarbinol with a b.p. of 95-97° (10 mm), d^{20}_4 0.8256, $n^{20}D$ 1.4330.

I. r.-spectrum (major frequencies): 729 s, 840 w, 905 w, 934 s, 947 s, 990 w, 1020 av, 1052 s, 1085 s, 1115 s, 1142 s, 1250 w, 1298 av, 1365 s, 1410 av, 1442 av, 1450 av, 1464 s cm^{-1}.

This same alcohol was obtained by the action of acetaldehyde on an ether solution of octylmagnesium bromide.

B.p. 95-97° (10 mm), d^{20}_4 0.8256, $n^{20}D$ 1.4300. Literature data [4]: b.p. 110-111° (10 mm).

The infrared spectrum was distinguished from the spectrum of the sample described above by having weaker bands in the 940 and 1290 cm^{-1} regions. Obviously, these differences are associated with the presence in the first sample of a slight amount of unsaturated alcohol, since the hydrogenation was not complete.

The two samples of 2-decanol were oxidized with sodium dichromate (10% excess) in acetic acid with dropwise addition of 50% sulfuric acid. The product in the two cases was the same—2-decanone, with the same constants, the same melting points of the semicarbazone and 2,4-dinitrophenylhydrazone, and practically superimposable infrared spectra.

B.p. 210-212° (765 mm), d^{20}_4 0.8236, $n^{20}D$ 1.4252. Semicarbazone: m.p. 123° (from aqueous alcohol). 2,4-Dinitrophenylhydrazone: m.p. 73° (from aqueous alcohol).

Literature data [5]: b.p. 209° (750 mm), d^{20}_4 0.8230, $n^{20}D$ 1.4263. Semicarbazone: m.p. 122-123°.

Mixed samples of the crystalline derivatives prepared from the two ketone samples melted at the same temperature as the pure substances.

I. r. spectrum of 2-decanone (major frequencies): 721 av, 967 w, 1016 vw, 1066 vw, 1118 w, 1163 s, 1219 av, 1242 av, 1281 w, 1360 s, 1414-1466 (apparently five strong frequencies), 1714 s, 1728 s cm^{-1} (Fig. 2, curve 1).

Addition of butyllithium to dimethylvinylacetylenylcarbinol. The reaction of 12 g of dimethylvinylacetylenylcarbinol with an ether solution of butyllithium by the usual method gave 14.5 g of an allenic alcohol with the constants given below, 3 g of a lower-boiling fraction, and 3 g of residue.

2-Methyl-3,4-decadien-2-ol. B.p. 96-97° (10 mm), d^{20}_4 0.8478, $n^{20}D$ 1.4640, MR 54.77; MR calc. 53.89.

Found %: C 78.48, 78.32; H 12.06, 12.04. $C_{11}H_{20}O$. Calculated %: C 78.51; H 11.98.

I. r. spectrum: 729 s, 764 av, 778 av, 837 w, 873 s, 894 s, 964 s, 1146 vs, 1238 s, 1337 s, 1361 s, 1406 s, 1446 s, 1461 s, 1600 w (diffuse), 1969 s, 2235 w, 2272 vw, 2863 s, 2928 s, 2963 s, 3400-3500 v.s. cm^{-1}.

During exhaustive hydrogenation of 3.2 g of the substance in 25 ml of methanol over colloidal palladium, 400 ml of H_2 (17.5°, 779 mm) was absorbed; this is about 87% of the calculated amount. There was obtained 2.6 g of dimethyloctylcarbinol.

B.p. 100-101° (10 mm), d^{20}_4 0.8243, $n^{20}D$ 1.4350.

I.r.-spectrum (major frequencies): 770 av, 910 s, 958 av, 1083 av, 1110 av, 1153 s, 1195 s, 1378 s, 1468 s cm^{-1}

The same alcohol was obtained by the action of acetone on octylmagnesium bromide.

B.p. 100-101° (10 mm), d^{20}_4 0.8238, $n^{20}D$ 1.4358. Literature data [6]: b.p. 82-83° (1-2 mm).

The i.r. spectrum of this substance was superimposable on the spectrum of the dimethyloctylcarbinol obtained by hydrogenation of the allenic alcohol without substantial deviations (Fig. 2, curve 2).

Addition of propyllithium to dimethylvinylacetylenylcarbinol. From 12 g of dimethylvinylacetylenylcarbinol and an ether solution of propyllithium was obtained 14 g of an allenic alcohol with the constants shown below, 2 g of a lower-boiling fraction, and 3 g of residue.

2-Methyl-3,4-nonadien-2-ol. B.p. 85-86° (10 mm), 97.5-98.5° (20 mm), d^{20}_4 0.8504, $n^{20}D$ 1.4640, MR 50.05, MR calc. 49.27.

Found %: C 77.88, 77.99; H 12.00, 11.86. $C_{10}H_{18}O$. Calculated %: C 77.86; H 11.76.

I. r. spectrum: 734 s, 743 s, 764 s, 783 av, 808 w, 872 s, 896 s, 966 s, 997 w, 1150 vs, 1239 s, 1373 vs, 1409 s, 1460 s, 1600 w (diffuse), 1974 s, 2244 vw, 2863 s, 2927 s, 2958 s, 3400-3500 vs cm^{-1}.

SUMMARY

1. The manner of addition of lithium alkyls to vinylalkylacetylenic alcohols—methyl- and dimethylvinylacetylenylcarbinol—were investigated.

2. It was shown that in all cases the reaction proceeds predominantly by 1,4-addition, and the alkyl group attaches to the terminal atom of the vinylacetylenic system.

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SYNTHESIS OF SUBSTITUTED CHROMONE-2-CARBOXYLIC ACIDS AND THEIR ESTERS

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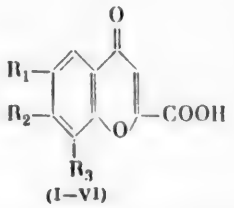
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3894-3898, December, 1960
Original article submitted November 20, 1959

Chromone-2-carboxylic acids with substituents in the benzene ring may be prepared by cyclization of the corresponding phenoxyfumaric acids (see, for example, references [1, 2]) or by condensation of substituted 2-hydroxyacetophenones with diethyl oxalate under the influence of sodium followed by cyclization of the resulting esters of o-hydroxybenzoylpyruvic acid to esters of chromonecarboxylic acid and hydrolysis of the latter (see, for example, references [3-5]).

Sodium ethylate has been used as the condensation catalyst in the synthesis of unsubstituted chromone-2-carboxylic acid [6]. The intermediate products, the sodium derivative of ethyl o-hydroxybenzoylpyruvate and of the ester of chromonecarboxylic acid, are separated by this method. If it is desired to obtain chromone-2-carboxylic acid directly, the process can be carried out without separation of the intermediate product [7].

The present communication describes the synthesis of substituted chromone-2-carboxylic acids (I-VI) by condensation of o-hydroxyacylbenzenes with diethyl oxalate in the presence of an alcohol solution of sodium ethylate.



(I—VI)

(I) R_1, R_3 = H, R_2 = CH_3;
(II) R_1, R_3 = H, R_2 = CH_3;
(III) R_2, R_3 = H, R_1 = Cl;
(IV) R_1, R_3 = H, R_2 = CH_3O;
(V) R_2, R_3 = H, R_1 = NO_2;
(VI) R_2 = H, R_1, R_3 = Br.

This same route has been used for the preparation of 3-methylchromone-2-carboxylic acid (VII). Like the unsubstituted ketone, 2-hydroxyacetophenones with CH_3, Cl, and CH_3O as substituents rather easily condense under the influence of 1 mole of sodium ethylate in alcohol [in the experiment with 5-methyl-2-hydroxyacetophenone, 1.5 moles of alcoholate was used in order to obtain the highest possible yield of acid (I)]. 3,5-Dibromo- and 5-nitro-2-hydroxyacetophenone undergo practically no condensation with diethyl oxalate in the presence of 1 mole of sodium ethylate; this is evidently due to the relatively high acidity of the phenolic hydroxyl. It was necessary to use 2 moles of sodium ethylate to carry out the condensation successfully.

In addition to substituted chromone-2-carboxylic acids, we also characterized a number of esters of these acids. The esters were prepared by esterification or by the condensation of o-hydroxyacylbenzenes as described above.

Under the synthesis conditions used for the unsubstituted chromone-2-carboxylic acid [7], certain of the intermediately formed esters do not hydrolyze completely, possibly owing to their poor solubility in the aqueous alcohol medium. For this reason, in the preparation of acids (V and VI) the corresponding esters were first separated in the free form, and were then hydrolyzed in a more appropriate medium.

We now direct attention to the fact that the condensation of o-hydroxypropiophenone with diethyl oxalate in the presence of 1 mole of sodium ethylate proceeds poorly. However, there is no doubt that the reason for this is the rather low acidity of the hydroxyl of o-hydroxypropiophenone and the decreased lability (in the sense of the ability to undergo protonization) of the hydrogen atoms at the alpha carbon. This latter effect is due to the electron donor effect of the methyl group. The condensation proceeds considerably better with 2 moles of sodium ethylate; nevertheless, a part of the hydroxypropiophenone is recovered unchanged, even after prolonged heating in the presence of a large excess of ethylate. This indicates that the condensation reaction is reversible.

We propose to carry out more detailed investigations of the effect of various factors on the ester condensation of hydroxyacetophenones.

EXPERIMENTAL

6-Methylchromone-2-carboxylic acid (I). To a solution of sodium ethylate (prepared from 1.38 g of sodium and 30 ml of anhydrous alcohol) was added, with stirring, a mixture of 6 g of 5-methyl-2-hydroxyacetophenone and 8.8 g of diethyl oxalate. The reaction mixture was heated at about 70° for 3 hr, and 8.4 ml of concentrated HCl was added (for cyclization of the ester of 5-methyl-2-hydroxybenzoylpyruvic acid). The mixture was refluxed for 30 min and then cooled. To the mixture was added 18.4 ml of concentrated HCl in 28 ml of water (to hydrolyze the ester), and the mixture was refluxed for an additional 3 hr. The precipitate which formed when the reaction mixture was cooled was filtered, washed with water, and dried. The yield was 5.4 g (66%) of acid (I), m.p. 258° (with decomposition; from alcohol). Reference [2] gives an m.p. of 258 (with decomposition).

In the experiments in which acids (II, III, IV, and VII) were prepared by the condensation method, the reagents were used in the following amounts: 1.5 mole of diethyl oxalate per mole of o-hydroxyacylbenzene; for the cyclization, 140 ml of concentrated HCl per gram atom of sodium introduced; for the hydrolysis, 460 ml of concentrated HCl plus 700 ml of water per mole of o-hydroxyacylbenzene.

Methyl ester of 6-methylchromone-2-carboxylic acid. A mixture of 8.17 g of acid (I), 80 ml of methanol, and 4 ml of concentrated sulfuric acid was refluxed for 3 hr and then cooled. The resulting crystals were removed by filtration and washed with an aqueous solution of sodium bicarbonate. The yield was 8.35 g (96%) of the methyl ester (including 0.75 g recovered from the methanol filtrate). The m.p. was 146.5-148° (from methanol).

Found %: C 66.08, 66.30; H 4.69, 4.58. $C_{12}H_{10}O_4$. Calculated %: C 66.05; H 4.62.

7-Methylchromone-2-carboxylic acid (II). This acid was prepared in a manner similar to that used for acid (I) from 0.15 mole of 4-methyl-2-hydroxyacetophenone and 0.17 mole of sodium ethylate in 150 ml of anhydrous alcohol.

Acid (II) (19.5 g), which was separated by the method described above was recrystallized from alcohol. An additional amount of the acid was separated from the mother liquor. This material was recrystallized from acetic acid. The over-all yield was 16.8 g (55%). M.p. 261° (with decomposition; from alcohol).

Found %: C 65.04, 64.89; H 4.18, 4.17. $C_{11}H_8O_4$. Calculated %: C 64.69; H 3.95.

Methyl ester of 7-methylchromone-2-carboxylic acid. This ester, prepared by direct esterification as described above, was obtained in 92% yield. The m.p. was 172-173.5° (from methanol).

Found %: C 65.80, 65.77; H 4.50, 4.43. $C_{12}H_{10}O_4$. Calculated %: C 66.05; H 4.62.

6-Chlorochromone-2-carboxylic acid (III). The reaction was carried out as in the preparation of acid (I) using 29.2 g of 5-chloro-2-hydroxyacetophenone and 4 g of sodium in 90 ml of anhydrous alcohol. The reaction product was separated by filtration and dissolved by shaking with aqueous $NaHCO_3$ and benzene. Acidification of the solution precipitated acid (III), which was separated by filtration, washed with water, and dried. It was treated with boiling dichloroethane (250 ml) and washed with dichloroethane and alcohol. The yield was 13.2 g (34%) of acid (III). The m.p. was 262° (with decomposition; from alcohol). Reference [1] reports an m.p. of 261-262° (with decomposition).

The benzene solution was evaporated and the residue was recrystallized from alcohol (containing carbon); 10.9 g (25%) of the ethyl ester of 6-chlorochromone-2-carboxylic acid was obtained. The m.p. was 136-136.5° (from alcohol).

Found %: Cl 14.05, 13.82. $C_{12}H_9O_4Cl$. Calculated %: Cl 14.03.

7-Methoxychromone-2-carboxylic acid (IV). This acid was prepared by the method previously described from 0.21 mole of 4-methoxy-2-hydroxyacetophenone and 0.21 g-at of sodium in 105 ml of alcohol. The yield was 74% (after treatment with boiling acetic acid). The m.p. was 270° (with decomposition; from CH_3COOH). Reference [3] gives an m.p. of 261° (with decomposition).

Ethyl ester of 6-nitrochromone-2-carboxylic acid. To a solution of sodium ethylate (prepared from 2.88 g of sodium and 50 ml of anhydrous alcohol) was added, with stirring, a warm solution of 9.05 g of 5-nitro-2-hydroxyacetophenone and 11 g of diethyl oxalate in 35 ml of alcohol. The reaction mixture was heated at 70° for 2 hr, then refluxed for 2.5 hr, and cooled. To the cooled solution was added 18 ml of concentrated HCl, and the mixture was refluxed for an additional 30 min. The mixture was cooled and allowed to stand for 16 hr, and the resulting precipitate was separated by filtration, washed with water and a solution of potassium bicarbonate, and dried. There was obtained 11.4 g (86%) of the ethyl ester. The m.p. was 178-179° (from alcohol).

Found %: N 5.53, 5.56. $C_{12}H_9O_6N$. Calculated %: N 5.32.

6-Nitrochromone-2-carboxylic acid (V). A mixture of 8 g of ethyl 6-nitrochromone-2-carboxylate, 32 ml of dioxane, and 19 ml of concentrated HCl was heated on a water bath for 4 hr. A precipitate formed when the solution was cooled, and this was separated by filtration and washed with water and chloroform. The yield of acid (V) was 6.7 g (94%). The m.p. was 268° (with decomposition; from aqueous alcohol).

Found %: N 6.11, 6.19, $C_{10}H_5O_6N$. Calculated %: N 5.96.

Ethyl ester of 6,8-dibromochromone-2-carboxylic acid. To a solution of sodium ethylate (prepared from 5.6 g of sodium and 120 ml of anhydrous alcohol) was added a mixture of 28.5 g of 3,5-dibromo-2-hydroxyacetophenone, 21 g of diethyl oxalate, and 80 ml of alcohol. The reaction mixture was heated at 60-70° for 3 hr, then refluxed for 1 hr, cooled, and, after the addition of 34 ml of concentrated HCl, refluxed again for 30 min. The mixture was allowed to stand for about 16 hr, and the resulting precipitate was separated by filtration, washed with water, and dissolved in chloroform in the presence of aqueous $NaHCO_3$. Distillation of the chloroform yielded 31.9 g (87%) of the ethyl ester of acid (VI). The m.p. was 134.5-135° (from alcohol).

Found %: Br 42.57, 42.36. $C_{12}H_8O_4Br_2$. Calculated %: Br 42.50.

From the bicarbonate solution was precipitated 2.1 g (6%) of 6,8-dibromochromone-2-carboxylic acid.

6,8-Dibromochromone-2-carboxylic acid (VI). Hydrolysis of 25 g of the ethyl ester was carried out by refluxing for 4 hr with a mixture of 150 ml of glacial CH_3COOH and 75 ml of concentrated HCl. The mixture was cooled, and the precipitate was separated by filtration and washed with water and chloroform. The yield of acid (VI) was 21.5 g (94%). The m.p. was 257° (with decomposition; from aqueous alcohol).

Found %: Br 45.98, 46.10. $C_{10}H_4O_4Br_2$. Calculated %: Br 45.92.

3-Methylchromone-2-carboxylic acid (VII) and its ethyl ester. The reaction was carried out as described for the preparation of acid (I) with 45 g of 2-hydroxypropiophenone and 13.8 g of sodium in 300 ml of alcohol (the time for the ester condensation was increased to 5 hr). The reaction product was recovered by filtration (precipitate A), washed with water and petroleum ether, and then dissolved by treatment with benzene and aqueous bicarbonate. Acid (VII) was precipitated from the bicarbonate solution. The crude acid (17.4 g) was purified by recrystallization from alcohol, and the yield was 12.75 g (including the acid recovered from the mother liquor). Distillation of the solvent from the benzene solution and recrystallization of the residue yielded 9.75 g of the ethyl ester of acid (VII). The filtrate and wash liquid from precipitate A were combined and extracted with benzene. Acid (VII) (2.3 g) was extracted from the benzene solution with aqueous bicarbonate, and was purified by recrystallization from alcohol. The yield was 0.75 g; the over-all yield of acid (VII) was 13.5 g (22%). The m.p. was 231.5 g (from alcohol). Reference [8] gives an m.p. of 233-234°.

The solvent was distilled from the benzene solution, and the unreacted hydroxypropiophenone (8.9 g) was then distilled under vacuum. An additional 7.75 g of the ethyl ester was separated from the distillation residue and the filtrates from the recrystallization of the ester. The over-all yield of ester was 17.5 g (25%). The m.p. was 93.5-94° (from alcohol). Reference [8] gives an m.p. of 89-90°.

SUMMARY

A number of substituted chromone-2-carboxylic acids and their esters were prepared by condensation of the appropriate o-hydroxyacylbenzenes with diethyl oxalate in the presence of an alcoholic solution of sodium ethylate.

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PECULIARITIES OF THE BROMINATION OF 1,1-DIPHENYL-2 BROMO-1-PROPANOL AND 1,1-DIPHENYL-2-BROMO-1-PROPENE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3898-3901, December, 1960
Original article submitted January 20, 1960

The bromination of 1,1-diphenyl-1-propanol (I) can vary depending on the conditions [1, 2]. In anhydrous solvents ($CHCl_3$, CCl_4, and CH_3COOH), the end product of the reaction is 1,1-diphenyl-2-bromo-1-propene (III).

$$(C_6H_5)_2COH-\underset{(I)}{CH_2}-CH_3 + Br_2 \longrightarrow (C_6H_5)_2COH-\underset{(II)}{CHBr}-CH_3 + HBr \longrightarrow$$
$$\longrightarrow [(C_6H_5)_2CBr-CHBr-CH_3] + HOH \longrightarrow \underset{(III)}{(C_6H_5)_2C=CBr-CH_3} + HBr$$

In 80% acetic acid, the reaction stops at the first stage with the formation of 1,1-diphenyl-2-bromo-1-propanol (II).

It seemed of interest to determine whether further replacement of the hydrogen atoms of this substance by bromine is possible and also to clarify the course of the reaction; both of these objectives were accomplished in the present work.

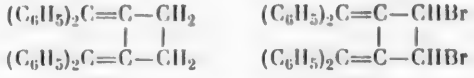
Bromination of 1,1-diphenyl-2-bromo-1-propanol (II) in chloroform proceeds smoothly under illumination by direct sunlight or ultraviolet light. During the reaction, there is copious evolution of hydrogen bromide, and an unstable, greenish, crystalline substance is formed, which on standing in air at room temperature, slowly loses HBr and is converted to a yellowish, crystalline material which proved to be 1,1-diphenyl-2,3-dibromo-1-propene (IV). This dibromide is a stable compound, but under the action of alcoholic alkali a molecule of hydrogen bromide is split out to form 1,1-diphenyl-3-bromopropadiene (V).

$$(II) \xrightarrow{+Br_2} [(C_6H_5)_2COH-CHBr-CH_2Br] + HBr \longrightarrow$$
$$\longrightarrow H_2O + [(C_6H_5)_2CBr-CHBr-CH_2Br] \longrightarrow HBr + \underset{(IV)}{(C_6H_5)_2C=CBr-CH_2Br} \longrightarrow$$
$$\xrightarrow[C_2H_5OH]{KOH} (C_6H_5)_2C=C=CHBr + HBr \qquad (V)$$

Oxidation of dibromide (IV) with nitric acid and of bromide (V) with potassium permanganate yields only benzophenone, which confirms the structures of these compounds.

We attempted to make use of the weakness of the carbon–bromine bond in unsaturated bromides (III) and (IV) to prepare 1,1-diphenylpropadiene, which has not been prepared up to the present. With this aim, we eliminated bromine from 1,1-diphenyl-2,3-dibromo-1-propene by means of magnesium in ether. The reaction proceeded vigorously, and 0.5 g-at of magnesium was consumed per mole of bromide. The product was a dark-red, oily liquid which was converted to a red-brown polymer during an attempt to distill it at 3 mm pressure.

The action of alcoholic alkali on 1,1-diphenyl-2-bromo-1-propene liberated almost the theoretical amount of potassium bromide, and two reaction products were formed—a dark red, oily liquid, which was the major product, and a little crystalline material. It was not possible to obtain these two substances as pure chemical individuals. An investigation of the crystalline substance suggested that it was a dimer of 1,1-diphenylpropadiene. This substance was converted by the action of bromine into a dibromide which contained bromine in the amount required for a dimer of 1,1-diphenylpropadiene. On the basis of the investigations of S. V. Lebedev [3] of dimers of unsymmetrical dimethylallene, the structures of our 1,1-diphenylpropadiene dimer and its dibromide can probably be represented by formulas (VI) and (VII).



(VI) (VII)

EXPERIMENTAL

1,1-Diphenyl-2-bromo-1-propanol (II) was prepared by the action of bromine on 1,1-diphenyl-1-propanol in 80% acetic acid [1].

The action of bromine on 1,1-diphenyl-2-bromo-1-propanol. (Preparation of 1,1-diphenyl-2,3-dibromo-1-propene) (IV). A solution of 6 g of bromohydrin (II) in anhydrous chloroform was prepared, and 4 g of bromine was added. Disappearance of the bromine color was not observed. On the following day, the reaction mixture was subjected to the action of sunlight. Copious evolution of hydrogen bromide was observed, but the solution remained a dark-red color. On the next day, the reaction mixture was washed with water, a solution of soda, and once more with water and dried with $MgSO_4$. Upon evaporation of the chloroform, a greenish brown, crystalline material remained, which gave off HBr. The liberation of hydrogen bromide practically ceased within 2 days, and the crystals acquired a light yellow color. The substance was readily soluble in acetone and chloroform and difficultly soluble in alcohol. After recrystallization from a mixture of acetone and alcohol, the substance was almost white and had an m.p. of 88-89°.

Found %: Br 45.47. M 334, 339. $C_{15}H_{12}Br_2$. Calculated %: Br 45.43. M 351.8.

The substance did not contain active hydrogen.

Oxidation of 1,1-diphenyl-2,3-dibromo-1-propene with nitric acid. A mixture of 10 g of dibromide (IV) and nitric acid (25 ml NHO_3, d 1.38, and 25 ml of water) was refluxed for 3 hr, bromine being liberated during 40 min of this time. The reaction mixture was treated in the usual manner. A little oily material was separated from the neutral products of the oxidation. This material had the odor of benzophenone, and was converted by reaction with semicarbazide to a semicarbazone with an m.p. of 164-165°. A mixture with a sample of benzophenone semicarbazone showed no depression of the melting point. The identity of the other reaction products was not established.

The action of alcoholic alkali on 1,1-diphenyl-2,3-dibromo-1-propene. (Preparation of 1,1-diphenyl-3-bromopropadiene) (V). To an alcoholic solution of 20 g of dibromide (IV) was added 60 g of alcoholic potassium hydroxide (20 g of KOH and 40 g of alcohol). When this mixture was heated slightly on a water bath, potassium bromide was precipitated, and the solution became dark red. Dilution of the reaction mixture with water caused separation of a dark red, oily substance, which was extracted with ether and dried with Mg SO_4. Distillation under vacuum yielded 14.8 g of a thick, yellowish liquid having a mushroom-like odor. The b.p. was 169-171° (3 mm). The substance rapidly crystallized. The m.p. was 60-61° (from ethanol).

Found %: Br 29.31. M 281.9, $C_{15}H_{11}Br$. Calculated %: Br 29.49. M 270.9.

Oxidation of 1,1-diphenyl-3-bromopropadiene with potassium permanganate. To a solution of 4 g of bromide (V) dissolved in 150 ml of acetone (the acetone was preliminarily refluxed with $KMnO_4$ for 8 hr) was gradually added, with stirring, 10.8 g of finely ground potassium permanganate; the reaction mixture was cooled with ice water during the addition. Oxidation proceeded very slowly and reduction of the oxidizing agent was almost complete only after 7 days. The reaction mixture was treated in the usual manner. The presence of benzophenone among the neutral products of the reaction was established. The semicarbazone melted at 165-166°. A

mixture of this semicarbazone with benzophenone semicarbazone showed no depression of the melting point. A small amount of acetic acid was detected in the volatile acids; this was undoubtedly formed by oxidation of the acetone.

Bromination of 1,1-diphenyl-2-bromo-1-propene. To 4.5 g of unsaturated monobromide (III) in chloroform was added 2.6 g of bromine. The interaction of the halogen with the bromide proceeded smoothly under illumination by sunlight; hydrogen bromide was eliminated during the reaction. Upon evaporation of the chloroform there remained a yellow-orange, crystalline substance, which liberated hydrogen bromide. When the liberation of HBr had ceased, the substance was recrystallized from a mixture of alcohol and acetone. There was obtained 3.1 g of white crystals with an m.p. of 87-88°. A mixture of this substance with that obtained by bromination of bromohydrin (II) [1,1-diphenyl-2,3-dibromo-1-propene (IV)] showed no depression of the melting point.

The action of alcoholic alkali on 1,1-diphenyl-2-bromo-1-propene. To 20 g of bromide (III) dissolved in 40 g of alcohol was added 40 g of alcoholic KOH (1 part of base in 2 parts of alcohol), and the mixture was heated in a flask fitted with a reflux condenser for 12 hr on a water bath. Potassium bromide was precipitated during the heating. The reaction mixture was then diluted with water, and a dark red oily liquid separated; this was extracted with ether. The ether solution was dried, and the solvent was distilled under vacuum. We were unable to separate an individual compound from the residue. In addition to the liquid material, there was also formed 2.2 g of white crystals, which were insoluble in ether and alcohol, but which dissolved in acetone and benzene on heating and in chloroform at room temperature. The m.p. was 189-190°.

Found %: C 93.98; H 6.67. M 327.7, 336.8. $C_{30}H_{24}$. Calculated %: C 93.75; H 6.25; M 3.84.

An attempt to improve the analytical results by a second recrystallization were not successful.

The action of bromine on diphenylpropadiene dimer. To a solution of 4.7 g of the material in chloroform was slowly added 4.0 g of bromine. The bromine was rapidly decolorized, but there was a simultaneous evolution of HBr, and the solution acquired a dark green color. The reaction products were washed with a solution of potassium carbonate and then with water, and dried with $CaCl_2$. The mixture was filtered, and the chloroform was evaporated from the transparent, orange-colored solution. After some time, a white, crystalline substance separated; m.p. 140-141° (from alcohol).

Found %: Br 28.78. M 522.8. $C_{30}H_{22}Br_2$. Calculated %: Br 29.52; M 542.0.

SUMMARY

1. The bromination of 1,1-diphenyl-2-bromo-1-propanol and of 1,1-diphenyl-2-bromo-1-propene proceeds by substitution of bromine for the hydrogen atom attached to the tertiary carbon atom. The same product is formed in the two cases—1,1-diphenyl-2,3-dibromo-1-propene.

2. The action of alcoholic alkali on 1,1-diphenyl-2,3-dibromo-1-propene yields 1,1-diphenyl-3-bromopropadiene.

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OXIDATION OF HYDROCARBONS CONTAINING CONJUGATED DOUBLE BONDS BY ORGANIC PEROXY ACIDS

III. MECHANISM OF THE OXIDATION OF UNSYMMETRICAL ALKYL-1,3-DIENES BY ACETYL HYDROPEROXIDE

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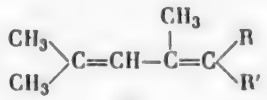
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3901-3907, December, 1960
Original article submitted December 29, 1959

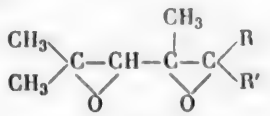
The oxidation of unsymmetrical alkyl-1,3-dienes (I) by acetyl hydroperoxide always leads to the formation of two different products, the products formed depending on the quantitative relationship between the hydrocarbon and the hydroperoxide [1, 2].



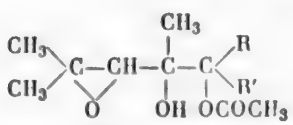
(I)

R = H, CH_3; R′ = Alk.

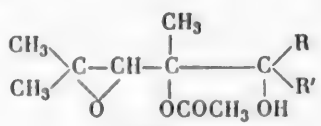
When 1 mole of hydrocarbon interacts with 2 moles of the hydroperoxide, oxidation takes place at both double bonds, and the reaction products are a diepoxy compound (II) and the monoacetate of an epoxydiol which may have one of the structures (III)-(VIII).



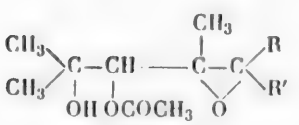
(II)



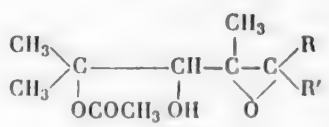
(III)



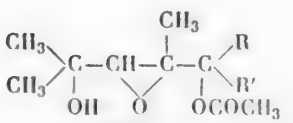
(IV)



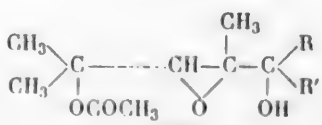
(V)



(VI)

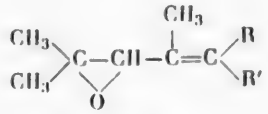


(VII)

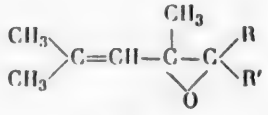


(VIII)

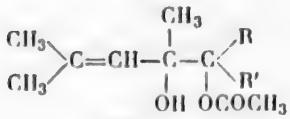
If the hydrocarbon and hydroperoxide are used in equimolar amounts, then only one double bond undergoes oxidation, and unsaturated monoepoxides and monoacetates of unsaturated diols are formed. The structure of the monoepoxide can be that of (IX) or (X), while the structure of the monoacetate may correspond to (XI)-(XVI):



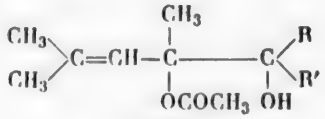
(IX)



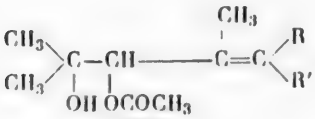
(X)



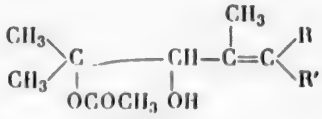
(XI)



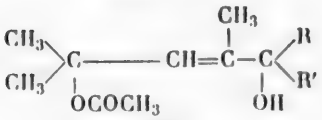
(XII)



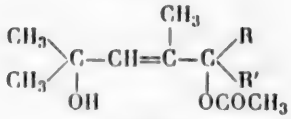
(XIII)



(XIV)



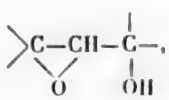
(XV)



(XVI)

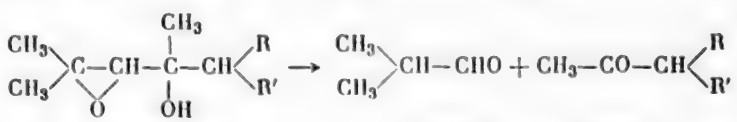
The present work was devoted to a further investigation of the structure of the products of this reaction, and the results will provide a basis for a more definite and more accurate opinion as to the mechanism of the oxidation of such hydrocarbons by acetyl hydroperoxide.

As may be seen from structures (III) and (VI)-(VIII), shown above, the structure of our epoxydiol monoacetates can include a hydroxyepoxide group. This group, which distinguishes α,β-hydroxyepoxides, is responsible for their ability, with very rare exceptions [3-7], to undergo cleavage at the C–C bond between the oxidized carbon atoms of the epoxide ring and the alcohol group under the influence of $ZnCl_2$, H_2SO_4, and other reagents with the formation of carbonyl compounds [8-21]. Thus, α,β-hydroxyepoxides (XVII), which have a carbon skeleton analogous to that of the epoxydiols investigated in the present work, are cleaved with the formation of isobutyraldehyde (XVIII) and the corresponding ketones (XIX) [18-21].



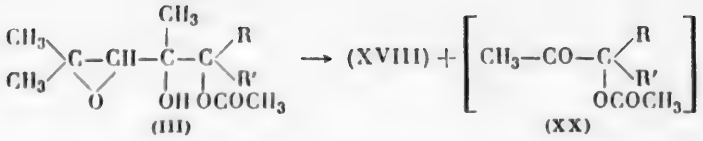
It would naturally be expected that epoxydiol monoacetates would also undergo cleavage under the action of zinc chloride, sulfuric acid, and other reagents in a manner similar to α,β-hydroxyepoxides.

As a matter of fact, epoxydiol monoacetates (XXVI) and (XXVII), which were prepared by oxidation of 2,4-dimethyl-2,4-pentadiene and 2,4-dimethyl-2,4-hexadiene [1, 2], do undergo cleavage with the formation of isobutyraldehyde when heated with anhydrous $ZnCl_2$. The formation of this aldehyde probably occurs in the present case, because the epoxydiol monoacetates have the structure (III):



(XVII) (XVIII) (XIX)

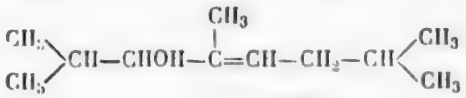
The presence of other oxidation products – acetates of α-hydroxyketones (XX) – was not established.



(III) (XX)

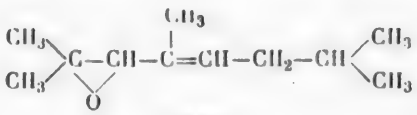
The unsaturated monoepoxide (XXI) and the unsaturated diol monoacetate (XXII) were obtained by oxidation of 2,4,7-trimethyl-2,4-octadiene with 1 mole of acetyl hydroperoxide. The structures of these two substances were established by hydrogenation and subsequent oxidation of the hydrogenation products with an aqueous solution of potassium permanganate.

In the hydrogenation of the monoepoxide, the addition of hydrogen took place at the oxide ring, and the double bond remained untouched. The hydrogenation product was an unsaturated alcohol, oxidation of which by potassium permanganate gave acetic, isobutyric and isovaleric acids. These substances could have been formed only by oxidation of 2,4,7-trimethyl-4-octen-3-ol (XXIII).



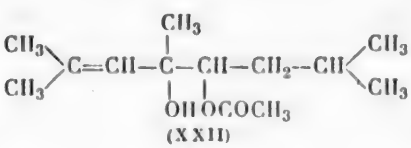
(XXIII)

Consequently, the monoepoxide obtained by oxidation of 2,4,7-trimethyl-2,4-octadiene by acetyl hydroperoxide is 2,4,7-trimethyl-2,3-epoxy-4-octene (XXI), and all of the monoepoxides obtained have the structure (IX).



(XXI)

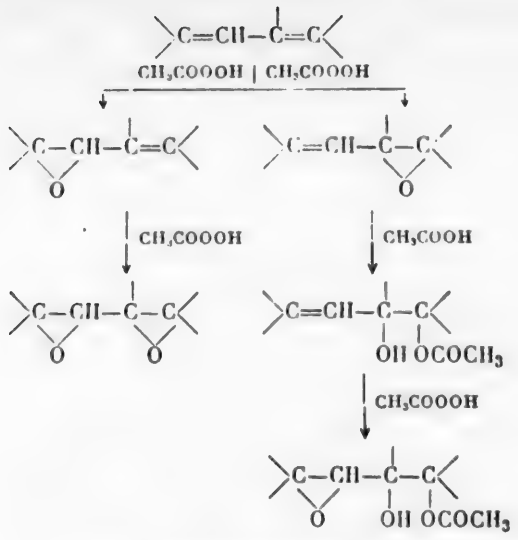
In the hydrogenation of the unsaturated diol monoacetate (XXII) over PtO_2, the hydrogen added across the double bond to yield a saturated diol acetate. When this compound was oxidized by potassium permanganate, the oxidation products were isovaleraldehyde, methyl isobutyl ketone, isovaleric acid, and acetic acid. These substances could have been formed by oxidation of alcohols resulting from hydrogenation of monoacetates having the structures (XI) and (XII). Since the most probable structure of the epoxydiol monoacetates is (III), the unsaturated diol monoacetate obtained by oxidation of 2,4,7-trimethyl-2,4-octadiene by acetyl hydroperoxide is 2,4,7-trimethyl-5-acetoxy-2-octene (XXII), and the monoacetates of the remaining unsaturated diols correspond to formula (XI).



(XXII)

Thus, the results of the present investigation show that the oxidation by acetyl hydroperoxide of the unsymmetrical alkyl-1,3-dienes studied in the present work proceeds in two directions simultaneously; oxidation occurs in the 2,3- and 4,5-positions, apparently with the formation of the two corresponding unsaturated monoepoxides. Further oxidation by acetyl hydroperoxide of the monoepoxides with the epoxide ring at the 2,3-position yields diepoxides. Monoepoxides with the epoxide ring at the 4,5-position are probably acetylated [22, 23] with the formation of monoacetates of unsaturated diols, which, upon further oxidation by hydroperoxide, yield monoacetates of epoxydiols.

Contrary to our previously proposed reaction scheme [2], these reactions probably occur in accordance with the scheme:



EXPERIMENTAL

Interaction of 2,4-dimethyl-5-acetoxy-2,3-epoxy-4-pentanol with zinc chloride. To 2 g of the epoxydiol monoacetate [2] was added 0.5 g of powdered anhydrous $ZnCl_2$, and the mixture was heated on a boiling water bath. The odor of isobutyraldehyde was apparent. The reaction products were dissolved in dimedon , and the solution was then heated on a boiling water bath for 2 hr. Crystals with an m.p. of 150-151° (from alcohol)[18] had formed by the following day. A mixture of this material with the dimedon addition product formed by isobutyraldehyde melted at the same temperature.

Interaction of 2,4-dimethyl-5-acetoxy-2,3-diepoxy-4-hexanol with zinc chloride. When 6 g of the epoxydiol monoacetate [1] was heated with 0.5 g of powdered anhydrous $ZnCl_2$, the odor of isobutyraldehyde was detected. The reaction products were collected in a solution of dimedon. After this solution had been heated, crystals with an m.p. of 150-151° (from ethanol) formed. A mixture of these crystals with the dimedon addition product formed by isobutyraldehyde showed no depression of the melting point.

It should be remarked that when 2,4-dimethyl-4,5-diacetoxy 2,3-epoxyhexane, previously prepared by us [1], was reacted with anhydrous zinc chloride under the same conditions, isobutyraldehyde was not formed.

Oxidation of 2,4,7-trimethyl-2,4-octadiene by acetyl hydroperoxide. The hydrocarbon was prepared by dehydration of 2,4,7-trimethyl-2-octen-4-ol [1]. To 94 g of the hydrocarbon dissolved in twice its volume of anhydrous ether was slowly added, at a temperature not exceeding 23°, 52 g of 91.8% acetyl hydroperoxide. The reaction proceeded vigorously, and was practically complete immediately after the addition of the hydroperoxide. The mixture was allowed to stand for 2 days, and the reaction products were then treated in the manner described in our preceding communications [1, 2]. Distillation under vacuum yielded two substances. One of them was obtained in a yield of 22.4 g. It was a mobile, colorless liquid with an agreeable odor.

B.p. 52-53° (2 mm), $n^{20}D$ 1.4390, d^{20}_4 0.8342, MR_D 52.97; calc. 52.10. The material contained no active hydrogen.

Found %: C 78.76; H 11.70. $C_{11}H_{20}O$. Calculated %: C 78.55; H 11.98.

The yield of the second substance (XXII) was 29.1 g. It was an oily liquid, which readily decolorized a solution of potassium permanganate and was soluble in organic solvents.

B.p. 107-112° (1.5 mm), $n^{20}D$ 1.4557, d^{20}_4 0.9623, MR_D 64.37; calc. 64.95.

Found %: C 68.38; H 10.53; OH 7.93. M 234. $C_{13}H_{24}O_3$. Calculated %: C 68.39; H 10.60; OH 7.45. M 228.

Hydrogenation of the monoepoxide 2,4,7-trimethyl-2,3-epoxy-4-octene (XXI). To 15.9 g of the monoepoxide dissolved in 40 ml of anhydrous alcohol was added 0.2 g of PtO_2, and hydrogen was passed through the mixture, which was agitated in a bomb at 25°. A total of 3750 ml of hydrogen was absorbed in a period of 3 hr (the amount theoretically required is 4240 ml). Since further absorption of hydrogen took place extremely slowly,

the catalyst was separated by filtration and washed with dry ether, and the reaction products were dried with a mixture of $MgSO_4$ and K_2CO_3. The solvent was distilled under vacuum, and the hydrogenation products were then distilled. There was obtained 5 g of a substance which had an agreeable odor, decolorized a solution of potassium permanganate, and, according to oxidation data, was an unsaturated alcohol (XXIII).

B.p. 66-68° (2 mm), $n^{20}D$ 1.4361, d^{20}_4 0.8333, MR_D 53.44; calc. 54.06.

Found %: C 77.81; H 13.07; OH 9.62. $C_{11}H_{22}O$. Calculated %: C 77.58; H 13.01; OH 9.98.

Oxidation of 2,4,7-trimethyl-4-octen-3-ol (XXIII) by potassium permanganate. An emulsion was formed with 4.02 g of the alcohol and 50 ml of water, and 3.3 g of $MgSO_4 \cdot 7H_2O$ and 370 ml of a 1% solution of potassium permanganate were added. The oxidation at first proceeded rapidly with evolution of heat; therefore, the mixture was cooled with ice water, and reduction of the oxidizing agent was then slowly completed over a period of 25 days. A volatile layer collected on the surface of the reaction mixture. This material had an agreeable odor. The aqueous solution of oxidation products had the odor of butyric acid. The reaction products were treated in the usual manner. Among the volatile, neutral oxidation products was 1.5 g of a substance which was apparently the starting material. Other neutral substances were not identified. A test of the solution of volatile acids for formic acid was negative. The following three fractions of silver salts of the volatile acids were obtained; the acids were isovaleric, isobutyric, and acetic.

1st fraction (%): Ag found, 51.53; calculated for $C_5H_9O_2Ag$, 51.64

2nd fraction (%): Ag found, 55.68; calculated for $C_4H_7O_2Ag$, 55.35

3rd fraction (%): Ag found, 64.67; calculated for $C_2H_3O_2Ag$, 64.64.

Hydrogenation of the unsaturated glycol monoacetate 2,4,7-trimethyl-5-acetoxy-2-octene-4-ol (XXII). To 20.95 g of the monoacetate dissolved in 50 ml of anhydrous alcohol was added 0.12 g of PtO_2. The mixture was agitated mechanically, and hydrogen was passed through it at 20-25°. The first 1000 ml of hydrogen was absorbed rapidly, while the second half of the hydrogen was absorbed slowly. Over a period of 2 hr, 2080 ml of hydrogen was introduced (2060 ml is the calculated amount required). At the conclusion of the hydrogenation, the catalyst was removed by filtration and washed with ether, and the hydrogenation products were dried with $MgSO_4$. The solvent was distilled under vacuum, and the reaction products were then distilled. There was obtained 6.8 g of a substance which, according to the results of the oxidation experiment, was 2,4,7-trimethyl-5-acetoxyoctanol.

B.p. 117-120° (2.5 mm), $n^{20}D$ 1.4473, d^{20}_4 0.9519, MR_D 64.69; calc. 65.41.

Found %: C 67.87; H 11.04. $C_{13}H_{20}O_3$. Calculated %: C 67.76; H 11.38.

Oxidation of 2,4,7-trimethyl-5-acetoxy-4-octanol by potassium permanganate. To an emulsion of 6.5 g of the alcohol obtained by hydrogenation of unsaturated diol monoacetate (XXII) in 50 ml of water was gradually added 300 ml of a 1% solution of $KMnO_4$. Oxidation proceeded rapidly, especially during the addition of the second half of the oxidizing agent. The reaction products were treated in the usual manner. The presence of two substances among the neutral oxidation products was established. One, which was steam distilled from the filtrate, proved to be an aldehyde, the adduct of which with dimedon melted at 155°. A mixed sample with the dimedon addition product formed by isovaleraldehyde showed no depression of the melting point. The second substance was separated from the distillate obtained by steam treatment of the manganese dioxide residue. The semicarbazone of this substance melted at 130-132° which corresponds to the melting point of methyl isobutyl ketone semicarbazone [24, 25]. The solution of volatile acids was heated with silver carbonate, and three fractions of salts were obtained. The first fraction was the silver salt of isovaleric acid, and the third fraction was the silver salt of acetic acid.

1st fraction (%): Ag found, 51.76; calculated for $C_5H_9O_2Ag$, 51.64.
2nd fraction (%): Ag found, 63.64.
3rd fraction (%): Ag found, 64.29; calculated for $C_2H_3O_2Ag$, 64.64.

SUMMARY

1. It was confirmed that the oxidation by acetyl hydroperoxide of unsymmetrical alkyl-1,3-dienes takes place simultaneously in two directions with the formation of different reaction products. The particular products formed depend on the quantitative relationship between the hydrocarbon and the hydroperoxide.

2. The structures of the oxidation products were established.

3. Our previously proposed reaction scheme for the oxidation by acetyl hydroperoxide of unsymmetrical alkyl-1,3-dienes has been corrected.

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TERTIARY TRIHYDRIC ALCOHOLS OF THE ACETYLENIC SERIES AND THEIR REACTIONS

XXI. DEHYDRATION OF 2,3,6-TRIMETHYL-4-OCTYNE-2,3,6-TRIOL AND 3,4,7-TRIMETHYL-5-NONYNE-3,4,7-TRIOL

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3907-3915, December, 1960
Original article submitted January 23, 1960

Some time ago, one of us together with A. Kh. Khamatov described the action of dehydrating agents on certain tertiary acetylenic 1,2,5-triols [1]. It was shown during the course of this work that dehydration takes place chiefly with the formation of substituted α-glycols of the vinylacetylene series. Substituted dienynols are formed, though in considerably smaller amount, as a result of elimination of two molecules of water from the triol molecule.

In the present work, dehydration of two other tertiary acetylenic triols was studied—2,3,6-trimethyl-4-octyne-2,3,6-triol (I) and 3,4,7-trimethyl-5-nonyne-3,4,7-triol (VII); these triols were first synthesized by one of us together with S. D. Savranskaya [2].

The acetylenic trihydric alcohol 2,3,6-trimethyl-4-octyne-2,3,6-triol (I) was dehydrated with potassium bisulfate, with p-toluenesulfonic acid, and with 30% sulfuric acid. Dehydration with sulfuric acid was accompanied by considerable tarring of the reaction products, and the over-all yield of the latter did not exceed 15%. Dehydration with p-toluenesulfonic acid and with potassium bisulfate led to the formation of two substances: a dienynol, 2,6-dimethyl-3-methylene-6-octen-4-yn-2-ol (II), and an α-glycol, 2,4,6-trimethyl-6-octen-4-yne-2,3-diol (III). The major dehydration product is dienynol (II), which is formed in 31% yield during dehydration with potassium bisulfate and 58% yield during dehydration with p-toluenesulfonic acid; the corresponding yields of α-glycol (III) were 12 and 8% (Scheme 1).

The structure of dienynol (II) was proved by oxidation with potassium permanganate, which yielded acetone and formic, acetic, oxalic, and α-hydroxyisobutyric acids. Propionic acid was not detected, which indicates that elimination of the hydroxyl from the 5-position removed a hydrogen from the ethyl, not the methyl radical.

Rate curves (Fig. 1) for the hydrogenation of dienyne carbinol (II) were constructed by the method of S. V. Lebedev both for hydrogenation over platinum (curve 1) and for hydrogenation over palladium deposited on calcium carbonate (curve 2). These curves show that after rapid addition of the first three moles of hydrogen, the rate dropped sharply during addition of the fourth mole. Assuming that selective hydrogenation to the ethylenic derivative is possible, we carried out the hydrogenation of dienyne carbinol (II) with the calculated amount of hydrogen (3 moles) in the hope of being able to isolate the ethylenic compound. However, we were unable to isolate an individual compound. Judging from the elemental analysis of certain fractions, hydrogenation proceeded in several directions with the formation of a mixture of dienyne, ethylenic, and saturated carbinols.

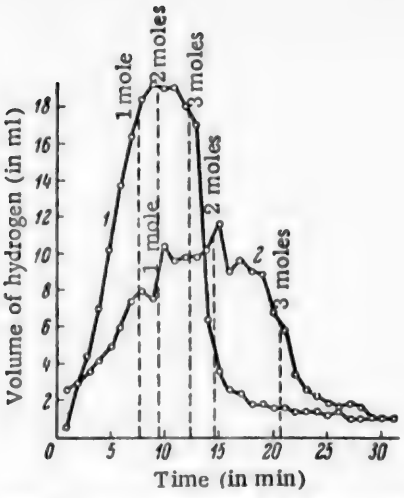


Fig. 1. Hydrogenation of 2,6-dimethyl-3-methylen-6-octen-4-yn-2-ol (II). 1) With 0.008 g of platinum oxide (17°), 2) with 0.08 g of palladium (20°).

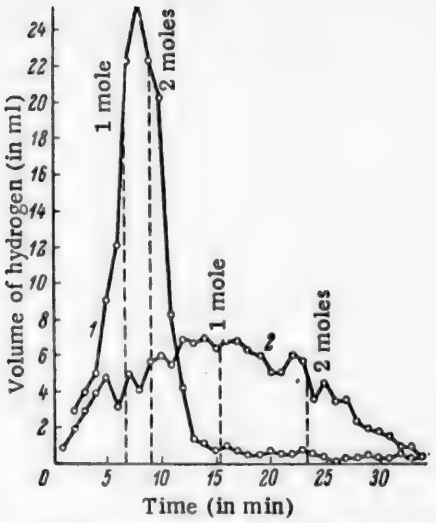
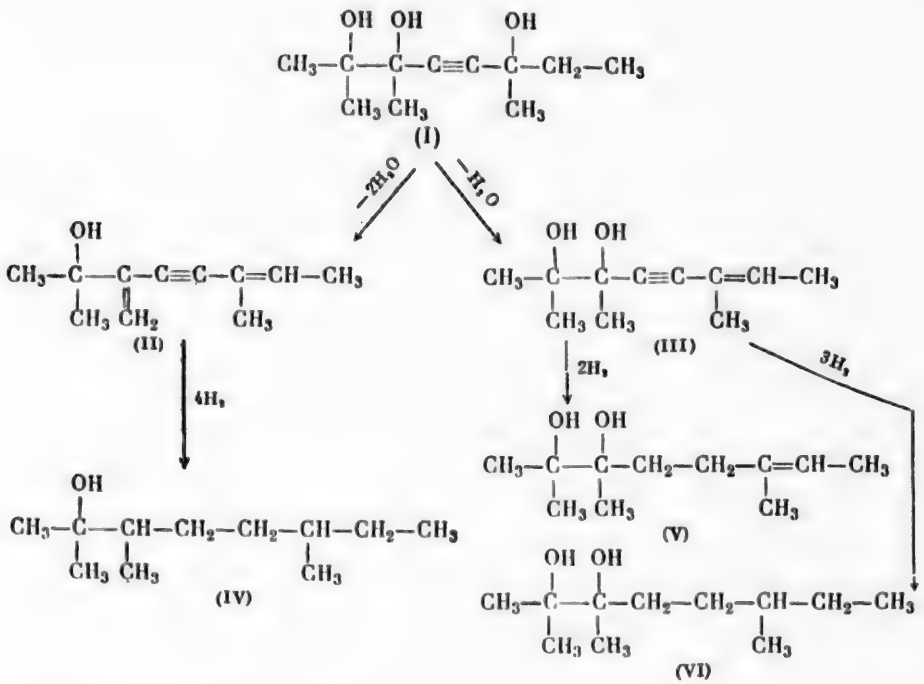


Fig. 2. Hydrogenation of 2,3,6-trimethyl-6-octen-4-yne-2,3-diol (III). 1) With 0.008 g of platinum oxide (17.5°), 2) with 0.08 g of palladium (18°).

Scheme 1



Exhaustive hydrogenation of 2,6-dimethyl-3-methylen-6-octen-4-yn-2-ol (II) yielded a saturated carbinol—2,3,6-trimethyl-2-octanol (IV).

The structure of the 2,3,6-trimethyl-6-octen-4-yne-2,3-diol (III) was proved by oxidation with potassium permanganate, which yielded acetone, dimethylacetylcarbinol, and formic, acetic, and oxalic acids.

When (III) was hydrogenated with the calculated amount of hydrogen (2 moles), we obtained 2,3,6-trimethyl-4-octene-2,3 -diol (V). As shown by the hydrogenation rate curve (Fig. 2, curve 1), hydrogenation in methanol solution over platinum oxide practically ceased after the addition of two moles of hydrogen. Therefore, exhaustive hydrogenation of α-glycol (III) was carried out in an acetic acid medium over platinum oxide. This gave the saturated α-glycol 2,3,6-trimethyloctane-2,3-diol (VI).

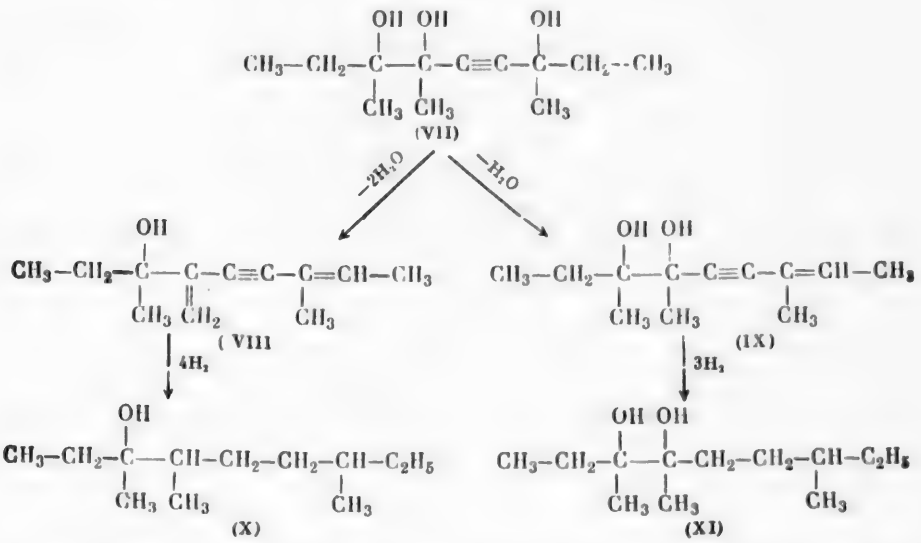
The dehydration of 3,4,7-trimethyl-5-nonyne-3,4,7-triol (VII) under the influence of potassium bisulfate also proceeded in two directions with the formation of the dienynol 3,7-dimethyl-4-methylene-7-nonen-5-yn-3-ol (VIII), the yield of which comprised 40%, and the enynediol 3,4,7-trimethyl-7-nonen-5-yne-3,4-diol (IX), the yield of which was 6% (Scheme 2).

When the dehydration was carried out with p-toluenesulfonic acid, the sole reaction product was dienynol (VIII) in a yield of 61%.

The structure of dienynol (VIII) was proved by oxidation with potassium permanganate. The oxidation yielded methyl ethyl ketone anf formic, acetic, oxalic, and methylethyl-α-hydroxyacetic acids.

Hydrogenation rate curves for dienynol (VIII), constructed as in the first case, are shown in Fig. 3; curve 1 is for hydrogenation over platinum oxide, and curve 2 is for hydrogenation over palladium deposited on calcium carbonate. They are similar to the rate curves for the hydrogenation of dienynol (II), which are shown in Fig. 1. The first of these curves shows that the hydrogenation of the dienynols continues at a certain rate after the addition of three moles of hydrogen, which indicates that ethylenic carbinols of this structure are capable of hydrogenation over both of the catalysts studied, and the hydrogenation proceeds at approximately the same rate for the two dienynols. Exhaustive hydrogenation of 3,7-dimethyl-4-methylene-7-nonen-5-yn-3-ol (VIII) gave 3,4,7-trimethyl-3-nonanol (X).

Scheme 2



In view of the small amount of material, oxidation of glycol (IX) was not attempted; however, on the basis of the analytical data and by analogy with the preceding investigations, we assign to it the structure 3,4,7-trimethyl-7-nonen-5-yn-3,4-diol (IX).

The rate curves for the hydrogenation of enynediol (IX) (Fig. 4) are also similar to the rate curves for the hydrogenation of enynediol (III). In this case, as may be seen from the curves, hydrogenation almost completely ceased after the addition of two moles of hydrogen, which brings up the possibility of isolating the corresponding α-glycol. Only in an acid medium (acetic acid solution) was it possible to carry the hydrogenation to the completely saturated glycol.

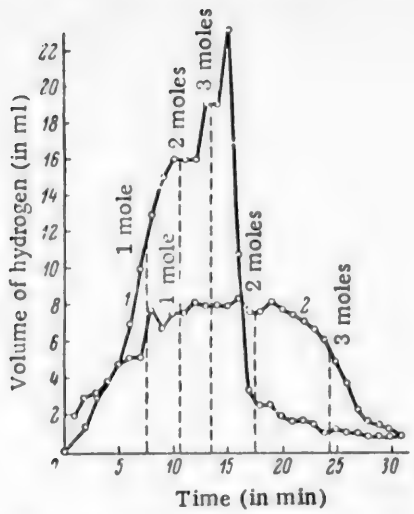


Fig. 3. Hydrogenation of 3,7-dimethyl-4-methylene-7-nonen-5-yn-3-ol (VIII). 1) With 0.008 g of platinum oxide (21°) 2) with 0.08 g of palladium (21.5°).

In the exhaustive hydrogenation of enynediol (IX), 3 moles of hydrogen were absorbed with the formation of 3,4,7-trimethylnonane-3,4-triol (XI).

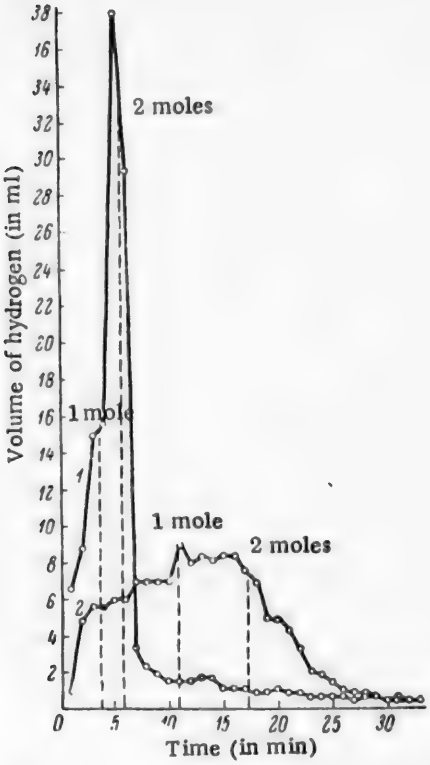
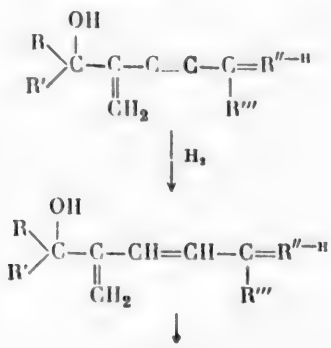


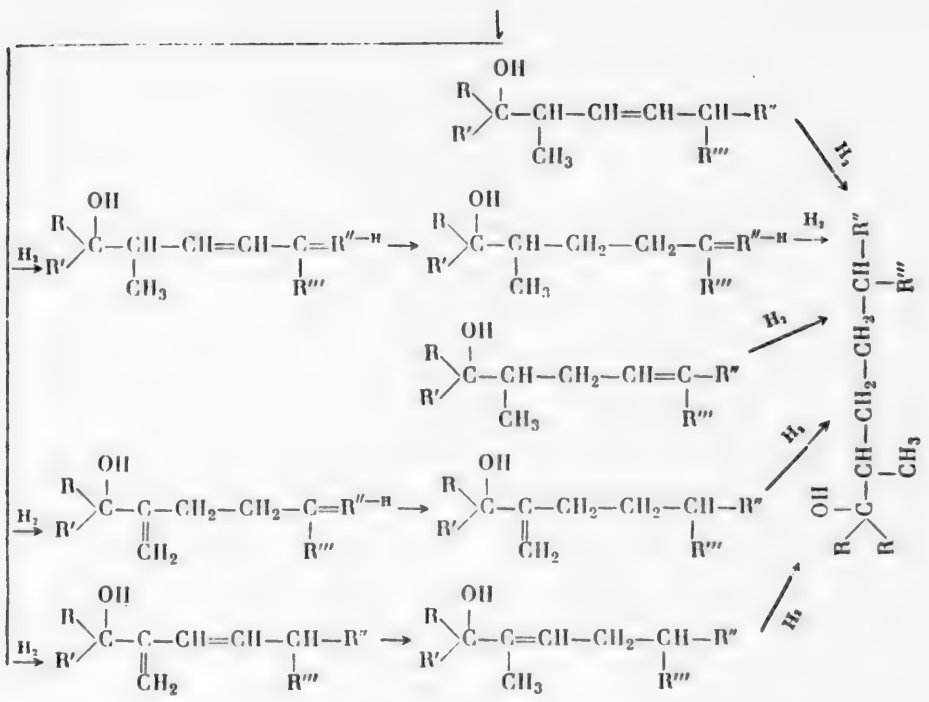
Fig. 4. Hydrogenation of 3,4,7-trimethyl-7-nonen-5-yne-3,4-diol (IX). 1) With 0.008 g of platinum oxide (16°), 2) with 0.08 g of palladium (25°).

Returning now to the question of the hydrogenation of dienyne carbinols (II) and (VIII), we may remark that these alcohols did not yield a unique ethylenic compound, in spite of the sharp decrease in the rate of hydrogenation after the addition of three moles of hydrogen. Judging from the elemental analysis of certain fractions of the hydrogenation products, these fractions comprised a mixture of dienyne, ethylenic, and saturated carbinols. Exhaustive hydrogenation did not lead to the formation of a single product. The explanation of this must be sought on the basis that hydrogenation of dienyne carbinols evidently proceeds through the formation of trienes, which subsequently undergo hydrogenation in various directions (Scheme 3). As a result, the formation of three diene carbinols would be expected. Further hydrogenation of the latter can give rise to the formation of up to five ethylenic carbinols. On the basis of the hydrogenation rate curves, the hydrogenation rate of the ethylenic carbinols is significantly lower than the rate of hydrogenation of the more unsaturated carbinols.

Thus, the ethylenic carbinols formed are further hydrogenated to saturation, but at a lower rate; consequently, selectivity of the hydrogenation to the formation of ethylenic carbinols is destroyed.

Scheme 3





EXPERIMENTAL

Dehydration of 2,3,6-Trimethyl-4-octyne-2,3,6-triol (I)

a) With potassium bisulfate. A mixture of 21.5 g of triol (I) (b.p. 121-122° at 1.5 mm), 8 g of potassium bisulfate, and 0.05 g of pyrogallol was heated in a flask at 135-140° on a Wood's metal bath. The mixture was distilled under a pressure of 3-4 mm, and 14.5 g of a fraction boiling at 88-89° was collected. The product was dissolved in ether and the ether solution was dried with sodium sulfate. During fractional distillation under vacuum, two fractions were collected: first fraction, b.p. 90-92° (8 mm), $n^{20}D$ 1.5092, 5.5 g (31%); second fraction, b.p. 110-111° (8 mm), $n^{20}D$ 1.4935, 2.5 g (12%).

b) With p-toluenesulfonic acid. A mixture of 22.3 g of the triol, 0.05 g of p-toluenesulfonic acid, and 0.05 g of pyrogallol was distilled under a pressure of 7-7.5 mm at a bath temperature of 140-145°. A total of 16.2 g of crude product was distilled; this material boiled at 87-104°.

A total of 78 g of material was dehydrated, and 57.8 g of dehydration products was obtained. Vacuum distillation of these products gave three fractions: first fraction, b.p. 86-88° (7 mm), $n^{20}D$ 1.5091, 36.9 g (57.5%); second fraction, b.p. 107-108° (7 mm), $n^{20}D$ 1.4939, 5.6 g (7.9%); third fraction, b.p. 108-109° (2 mm), 4.0 g; the third fraction was the original triol.

c) With sulfuric acid. When the triol was dehydrated over a period of 6 hr with 30% sulfuric acid at 65°, a large part of the material formed tar. The yield of dehydration product was about 15% of the triol.

The first fraction obtained by dehydration of the triol with p-toluenesulfonic acid was 2,6-dimethyl-3-methylene-6-octen-4-yn-2-ol (II); the second fraction was 2,3,6-trimethyl-6-octen-4-yne-2,3-diol (III).

Investigation of the First Fraction, b.p. 86-88° (7 mm)

d^{20}_4 0.8999, $n^{20}D$ 1.5091, MR_D 54.43. $C_{11}H_{16}OF_2E$. Calculated 57.79.

Found %: C 80.00, 80.00; H 9.56, 9.71; OH 10.52, 10.32. $C_{11}H_{16}O$. Calculated %: C 80.43; H 9.83; OH 10.36.

It was felt that the substance with a b.p. of 86-88° (7 mm) should be 2,6-dimethyl-3-methylen-6-octen-4-yn-2-ol (II), and this was confirmed by oxidation with potassium permanganate.

An 8.5 g sample of dienynol (II) was oxidized with 48 g of potassium permanganate (calculated on the basis of nine active oxygen atoms required per molecule of the material). The oxidation was carried out at room temperature with vigorous stirring. Over a period of 8 hr was added 600 ml of a 4% solution of permanganate. The remaining 24 g of oxidizing agent was introduced in small portions over a period of 5 hr. After the solution had become colorless, the manganese dioxide was removed by filtration and washed with hot water. A fraction containing the neutral products was distilled from the filtrate. This material was then distilled in a column, and 0.25 g of a fraction with a b.p. of 57-60° was obtained; reaction of this material with 2,4-dinitrophenylhydrazine gave acetone 2,4-dinitrophenylhydrazone with an m.p. of 126-128° (mixed melting point).

The salts of the acids were acidified, and the volatile acids were distilled. Neutralization of these acids required 3.6 g of sodium hydroxide. Qualitative tests for the presence of acetic (cacodyl oxide) and formic (precipitation by calomel) acids were positive.

Analysis of the mixture of silver salts of the volatile acids gave 65.80% Ag. The silver salt of formic acid was decomposed on heating. Analysis of the remaining silver salt gave 64.05% Ag. The calculated value for acetic acid is 64.65% Ag.

The silver content of the silver salt remaining after decomposition of the silver formate and also the negative reaction with lead acetate indicates the absence of propionic acid. Consequently, the elimination of hydrogen during dehydration takes place at the number 7 carbon atom and not from the methyl radical attached to the sixth carbon, which is in agreement with the Wagner–Zaitsev rule. From the volatile acids were isolated 2.6 g of oxalic acid with an m.p. of 101-102° (mixed melting point) and 1 g of α-hydroxyisobutyric acid with an m.p. of 78-79° (mixed melting point).

Thus, the products of the oxidation of dienynol (II) confirm its structure.

Hydrogenation of 12.8 g of 2,6-dimethyl-3-methylen-6-octen-4-yn-2-ol was carried out in 70 ml of methanol over 0.1 g of palladium deposited on calcium carbonate (hydrogenation conditions were 26.5° and 690.3 mm). The hydrogenation was stopped after the absorption of 6287 ml of hydrogen (which corresponds to 3 moles of hydrogen). The methanol was distilled, and the residue was dissolved in ether. The ether solution was dried over sodium sulfate, and the ether was distilled. We were unable to isolate an individual compound by vacuum distillation. Some of the fractions obtained in the distillation were analyzed for elemental composition, and the results indicated that hydrogenation of the dienyne carbinol occurred simultaneously in several directions, which excludes the possibility of any selectivity.

During exhaustive hydrogenation of 9 g of dienynol (II) in 50 ml of methanol over 0.1 g of palladium deposited on calcium carbonate (18.5° and 693 mm), 5500 ml was absorbed in 8 hr (the calculated amount for 4 moles is 5380). The methanol was distilled, and the crude product was dried with sodium sulfate and then distilled under vacuum. A second distillation yielded 7.0 g of 2,3,6-trimethyl-2-octanol (IV).

B.p. 89-90° (8 mm), d^{20}_4 0.8480, $n^{20}D$ 1.4449, MR_D 53.96; calc. 54.52.

Found %: C 76.23, 76.61; H 13.52, 13.54; OH 8.74, 8.56. $C_{11}H_{24}O$. Calculated %: C 76.76; H 13.95; OH 9.88.

Investigation of the Fraction Boiling at 107-108° (7 mm)

d^{20}_4 0.9524; $n^{20}D$ 1.4939, MR_D 55.54. $C_{11}H_{18}O_2FF$. Calculated 53.78.

Found %: C 72.46, 72.19; H 9.99, 9.96; OH 19.20, 18.88. $C_{11}H_{18}O_2$. Calculated %: C 72.46; H 9.96; OH 18.68.

A 9.5 g sample of the material was oxidized with 38.4 g of potassium permanganate (calculated on the basis of seven active oxygen atoms required per molecule of the material). A total of 700 ml of a 4% solution of $KMnO_4$ was added over a period of 6 hr, and then 10.4 of the finely ground oxidizing agent was introduced in small portions. Treatment of the oxidation products was as described above. Distillation of the neutral products in a column gave 0.5 g of acetone with a b.p. of 54-56°; the acetone was identified by its 2,4-dinitrophenylhydrazone, which had an m.p. of 126-128° (mixed melting point). A fraction boiling at 56-75° (0.7 g) was also collected, and from it was isolated dimethylacetylcarbinol semicarbazone with an m.p. of 160-162° (mixed melting point).

The distillate containing the volatile acids was neutralized with 2.9 g of sodium hydroxide. The presence of formic and acetic acids was demonstrated by qualitative tests with calomel and cacodyl oxide. The mixture of silver salts of the volatile acids analyzed 66.10% Ag.

The material remaining after decomposition of the silver formate analyzed: Ag found, 64.31%; calculated for CH_3COOAg, 64.65%.

Propionic acid was not detected. Oxalic acid, m.p. 101-102° (mixed melting point) was separated from the volatile acids.

Thus, the products of the oxidation of the fraction boiling at 107-108° (7 mm) were acetone, dimethylacetylcarbinol, and formic, acetic, and oxalic acids. On the basis of these data, we may take this fraction to be 2,3,6-trimethyl-6-octen-4-yne-2,3-diol (III).

Hydrogenation of 2.5 g of 2,3,6-trimethyl-6-octen-4-yne-2,3-diol (III) was carried out in 50 ml of benzene over 0.05 g of palladium deposited on calcium carbonate. The hydrogenation was stopped after the absorption of 720 ml of hydrogen (20°, 697.4 mm), which corresponds to 2 moles of hydrogen. The methanol was distilled, and the product was dried with potassium carbonate. Vacuum distillation of the product gave 1.8 g of a substance having the properties:

B.p. 74-75° (6 mm), d^{20}_4 0.9251, $n^{20}D$ 1.4638, MR_D 55.45. $C_{11}H_{22}O_2F$. Calculated 55.58.

Found %: C 71.34, 71.45; H 12.14; 11.93; OH 17.51, 17.78. $C_{11}H_{22}O_2$. Calculated %: C 70.96; H 11.83; OH 18.27.

In view of the small amount of this material, further investigations were not carried out with it, but by analogy to the preceding investigations, we consider it to be 2,3,6-trimethyl-6-octene-2,3-diol (V).

Exhaustive hydrogenation of the 2,3,6-trimethyl-6-octen-4-yne-2,3-diol (III) was carried out using 5.6 g of the freshly distilled diol in 35 ml of glacial acetic acid; the hydrogenation was catalyzed with 0.05 g of platinum oxide. The calculated amount of hydrogen, 2188 ml (16°, 693.1 mm) corresponding to 3 moles, was absorbed in 2 hr. The acetic acid was distilled under vacuum, and the product was neutralized with soda, dissolved in ether, and dried with potassium carbonate. Vacuum distillation yielded 5.0 g of 2,3,6-trimethyloctan-2,3-diol (VI).

B.p. 84-85° (1.5 mm), d^{20}_4 0.9177, $n^{20}D$ 1.4549, MR_D 55.58; calc. 56.04.

Found %: C 70.69, 70.44; H 12.77, 12.75; OH 18.04, 18.09. $C_{11}H_{24}O_2$. Calculated %: C 70.21; H 12.76; OH 18.08.

Dehydration of 3,4,7-Trimethyl-5-nonyne-3,4,7-triol (VII)

a) With potassium bisulfate. A mixture of 21.6 g of 3,4,7-trimethyl-5-nonyne-3,4,7-triol (VII), 6 g of potassium bisulfate, and 0.05 g of pyrogallol was distilled at a bath temperature of 140-156° and under a reduced pressure of 4 mm. The distillation yielded 16 g of dehydration products boiling in the range of 83 to 115°.

A total of 63.1 g of the triol was dehydrated, and 46.5 g of crude product was obtained. The product was dried with sodium sulfate and distilled under vacuum. Fractional distillation gave the following fractions: first fraction, 78-79° (3.5 mm), $n^{20}D$ 1.5065, 21.1 g (40%), which we found to be 3,7-dimethyl-4-methylene-7-nonen-5-yn-3-ol (VIII); second fraction, 103-103.5° (1.5 mm), $n^{20}D$ 1.4908, 3.5 g (6%), 3,4,7-trimethyl-7-nonen-5-yne-3,4-diol (IX).

b) With p-toluenesulfonic acid. A mixture of 21.1 g of triol (VII), 0.01 g of pyrogallol, and 0.02 g of p-toluenesulfonic acid was distilled at 142-150° under a reduced pressure of 7-8 mm. A total of 15.5 g of product boiling at 65-101° was distilled.

A total of 41.4 g of the triol was dehydrated, and 31.5 g of dehydration products was obtained. Fractional distillation under vacuum yielded only one pure fraction, in an amount of 21.1 g (61%), and this proved to be 3,7-dimethyl-4-methylene-7-nonen-5-yn-3-ol (VIII).

B.p. 86-87° (3 mm), d^{20}_4 0.8995, $n^{20}D$ 1.5073, MR_D 58.92. $C_{12}H_{18}O_2FF$. Calculated 56.20.

Found %: C 80.52, 80.61; H 11.05, 11.25; OH 9.39, 9.29. $C_{12}H_{18}O_2$. Calculated %: C 80.89; H 11.12; OH 9.55.

The dimethyl-4-methylene-7-nonen-5-yn-3-ol, 7 g, was oxidized with 37.3 g of potassium permanganate (calculated on the basis of nine active oxygens required per molecule of the material); 3.2 g of the potassium permanganate was added as a 4% solution, and 5.3 g was added in small portions in the form of a powder. After the usual treatment, the oxidation products were separated into two fractions: first fraction, 70-72°, 0.07 g; second fraction, 76-88°, 0.25 g. Both fractions yielded the 2,4-dinitrophenylhydrazone of methyl ethyl ketone, m.p. 111.5-112° (mixed melting point). The presence of formic and acetic acids was established in the steam-volatile acids; these acids required 2.25 g of NaOH for neutralization. Among the nonvolatile acids was found 0.8 g of oxalic acid, m.p. 101-102° (mixed melting point) and 1.6 g of methylethylhydroxyacetic acid, m.p. 71-72° (mixed melting point).

These oxidation products completely confirm the structure of the 3,7-dimethyl-4-methylene-7-nonen-5-yn-3-ol (VIII).

Hydrogenation of 5 g of dienynol (VIII) in 50 ml of methanol was carried out over 0.05 g of platinum oxide (28°, 691 mm). A total of 3200 ml of hydrogen was absorbed in 8 hr (calculated for 4 moles of hydrogen – 3017 ml). After the usual treatment, the hydrogenation products were distilled under vacuum. There was obtained 4.0 g of 3,4,7-trimethyl-3-nonanol (X).

B.p. 78-79° (3 mm), d^{20}_4 0.8558, $n^{20}D$ 1.4483, MR_D 58.61; calc. 59.15.

Found %: C 77.02, 77.03; H 14.01, 13.74; OH 8.63, 8.51. $C_{12}H_{24}O$. Calculated %: C 77.36; H 13.97; OH 9.13.

The second fraction obtained by dehydration of triol (VII) with potassium bisulfate was 3,4,7-trimethyl-7-nonen-5-yn-3,4-diol (IX).

B.p. 103-103.5° (1.5 mm), d^{20}_4 0.9579, $n^{20}D$ 1.4908, MR_D 59.24. $C_{12}H_{20}O_2$ F F. Calculated 58.20.

Found %: C 73.02, 72.98; H 10.14, 10.48; OH 16.32, 16.37. $C_{12}H_{20}O_2$. Calculated %: C 73.47; H 10.20; OH 17.34.

In view of the small amount of this material, it was not oxidized. The analytical data correspond to those obtained in previous investigations, and we assigned a structure to this substance on the basis of these investigations.

During the exhaustive hydrogenation of enynediol (IX) in glacial acetic acid over 0.1 g of platinum oxide (28°, 691.8 mm), 2200 ml of hydrogen was absorbed (this corresponds to 3 moles of hydrogen), and the hydrogenation practically ceased at this point. The acetic acid was distilled under vacuum, and the product was neutralized with soda and dried with potassium carbonate. Vacuum distillation of the product gave 3.27 g of 3,4,7-trimethylnonane-3,4-diol (X).

B.p. 103-104° (6 mm), d^{20}_4 0.9232, $n^{20}D$ 1.4581, MR_D 59.71; calc. 60.66.

Found %: C 71.22, 70.74; H 12.8, 12.8. $C_{12}H_{24}O_2$. Calculated %: C 71.28; H 12.32.

SUMMARY

1. Two acetylenic triols – 2,3,6-trimethyl-4-octyne-2,3,6-triol and 3,4,7-trimethyl-5-nonyne-3,4,7-triol – were dehydrated with potassium bisulfate and with p-toluenesulfonic acid.

2. The dehydration of triols in the presence of these hydrating agents proceeds in two directions yielding one product resulting from the elimination of one molecule of water from the triol – an α-glycol of the vinylacetylene series – and another product resulting from the elimination of two molecules of water – a divinylacetylenic carbinol. The second course predominates, and the yield of the vinylacetylenic carbinol is considerably increased by the use of p-toluenesulfonic acid. The sole product of the dehydration of the trimethylnonynetriol by p-toluenesulfonic acid is a dienyne carbinol, which was obtained in 61% yield.

3. Both dehydration products can be exhaustively hydrogenated to a saturated compound – the corresponding saturated carbinol and aliphatic α-glycol – by means of a platinum or palladium catalyst.

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SUBSTANCES WITH COMPLEX-FORMING ABILITIES

V. N,N,N',N'-TETRAACETIC ACID 2,2'-DIAMINODIETHYL ETHER

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3916-3918,
December, 1960
Original article submitted January 11, 1960

According to the information available in the literature [1], complexons containing hetero atoms (O, S, N) in a chain of methylene groups joining iminodiacetic acid residues possess highly effective complex-forming properties which are no less effective than ethylenediaminetetraacetic acid. In a continuation of our work devoted to the study of the synthesis and properties of complexons [2], we have synthesized tetraacetic acid 2,2'-diaminodiethyl ether. The preparation of this complexon has not been described in the literature; however, on the basis of patent information [3], it may be assumed that this complexon has been synthesized starting with 2,2'-diaminodiethyl ether by a carboxymethylation reaction. Nevertheless, the properties of the tetraacetic acid and of its salts were not described.

We initially attempted to synthesize the complexon by condensation of 2,2'-dibromodiethyl ether with an excess of the diethyl ester of iminodiacetic acid; however, we were unable to obtain positive results, and, therefore, we turned to the interaction of 2,2'-diaminodiethyl ether with chloroacetic acid. The diamino ether was prepared from 2,2'-dichlorodiethyl ether (Chlorex) by Gabriel synthesis through the diphthalimide derivative [4]. In place of heating the reactants with a mixture of concentrated hydrochloric and acetic acid in sealed tubes, decomposition of the 2,2'-di(phthalimido)diethyl ether was carried out by refluxing with an alcoholic solution of hydrazine hydrate and subsequent treatment with hydrochloric acid. This simplified the problem of carrying out the reaction, and it also gave higher yields. The diamine was separated in the form of the dihydrochloride, which was then reacted with monochloroacetic acid. An attempt to synthesize the 2,2'-diaminodiethyl ether from 2,2'-di(carbamido)diethyl ether by Hofmann reaction was unsuccessful; the action of hypochlorite and hypobromite on the diamide in water and in aqueous alcohol brought about only copious evolution of ammonia.

Condensation of the diamine dihydrochloride with monochloroacetic acid was carried out in the usual manner in alkaline medium [2]. Two methods were used for the isolation of the tetraacetic acid, which did not form a precipitate upon acidification of the reaction mixture, as certain other complexons do. In the first of these methods [5], the alkaline solution after dilution was passed through a KU-2 cation exchange resin in the acid form, and the column was eluted with water. After separation of the acid eluate, which contained chlorine ions, the acid fraction was collected; this fraction gave a positive reaction for complexon (murexide test). The tetraacetic acid dihydrate was separated by evaporation of this solution, and was purified by recrystallization from 50% alcohol.

In the other method, the reaction mixture was acidified to an acid reaction toward Congo indicator, and, after separation of the sodium chloride, the monosodium salt of the complexon was precipitated from the solution by means of methanol. It was purified by reprecipitation from aqueous methanol.

EXPERIMENTAL

2,2'-Di(phthalimido)diethyl ether. A mixture of 78.8 g of potassium phthalimide, 28.6 g of 2,2'-dichlorodiethyl ether, and 2 ml of diethylamine was heated, with stirring, for 4 hr at 140-150° (in the reaction mixture). During this time, 1 ml of diethylamine was twice added to the reaction mixture. The mixture was then cooled to 100°, and 400 ml of hot water was added; the mixture was refluxed for 20 min, and the precipitate was filtered. The precipitate was washed with water and dried in air, and 70 g (96.3%) of 2,2'-di(phthalimido)diethyl ether was obtained; m.p. 153-156°. The literature [4, 6] gives an m.p. of 156.5°.

2,2'-Diaminodiethyl ether dihydrochloride. A mixture of 54.6 g of the diphthalimido derivative, 15 g of 100% hydrazine hydrate and 250 ml of alcohol was refluxed, with stirring, for 2 hr, during which time a voluminous white precipitate was formed. After dilution with 50 ml of concentrated hydrochloric acid, the mixture was cooled to 0-5°, and the precipitate was separated by filtration and washed with 70 ml of alcohol. The filtrate and wash alcohol were decolorized with charcoal and evaporated to dryness under reduced pressure. The crystalline residue was treated with 50 ml of dry isopropyl alcohol and dried; and 20.6 g of 2,2'-diaminodiethyl ether dihydrochloride was obtained after the residue was dried. The yield was 77.5% (calculated on the diphthalimide derivative) and 74.5% (based on the Chlorex); the m.p. was 220-223° (from 96% alcohol). The literature [4] gives a value of 226-227° for the m.p.

Tetraacetic acid 2,2'-diaminodiethyl ether. To a solution of 28.6 g of monochloroacetic acid dissolved in 32 ml of a 30% solution of chemically pure sodium hydroxide was added 10.62 g of 2,2'-diaminodiethyl ether dihydrochloride, and about 45 ml of the 30% solution of base was gradually added at room temperature at a rate such that the pH of the solution remained constant at 10-11. When the addition was complete, the mixture was heated for 3 hr at 40° and then 3 hr on a boiling water bath. The solution was cooled to room temperature, diluted with a three-fold amount of distilled water, and passed at a rate of about 8 ml/min through a column (40 by 500 mm) containing 400 g of KU-2 resin treated with hydrochloric acid. When the column was eluted with distilled water, two acid fractions were obtained. The second of these (about 6 ml) gave a positive reaction for complexon (retention of the lilac color of an alkaline solution of murexide upon the addition of several drops of a calcium chloride solution).

The second solution was evaporated under reduced pressure, and the residue was recrystallized from 50% methyl alcohol. After drying in a vacuum desiccator over P_2O_5, the crystals of tetraacetic acid 2,2'-diaminodiethyl ether dihydrate weighed 12.74 g (85.5% yield, calculated on the dihydrochloride). The product was a white, finely crystalline powder which decomposed at about 135°.

Found %: C 38.67; H 6.56; N 7.81. $C_{12}H_{20}O_9N_2 \cdot 2H_2O$. Calculated %: C 38.72; H 6.45; N 7.53.

Drying of the dihydrate at 100° removed all of the water of crystallization, and the anhydrous tetraacetic acid was obtained; it decomposed at about 205°.

Found %: C 42.48; H 6.03; N 8.23. $C_{12}H_{20}O_9N_2$. Calculated %: C 42.86; H 6.00; N 8.33.

Monosodiumsalt of tetraacetic acid 2,2'-diaminodiethyl ether. To a solution of 17.7 g of 2,2'-diaminodiethyl ether dihydrochloride and 41.5 g of monochloroacetic acid in 50 ml of water at a temperature of about 40° was added gradually, with stirring, 44 g of powdered sodium hydroxide. The mixture was held at this temperature for 2 hr, and at room temperature for 12 hr. The reaction mixture was acidified with concentrated hydrochloric acid (30 ml) to an acid reaction toward Congo indicator, and the precipitated sodium chloride was separated by filtration and washed with 50 ml of 50% aqueous methyl alcohol. A two-fold volume of methanol was added, with stirring, to the filtrate and wash alcohol at a temperature of 40-45°; the resulting precipitate, which contained the monosodium salt of the complexon and a certain amount of sodium chloride, was removed by filtration and again dissolved in 100 ml of water. The solution was again treated with a two-fold volume of methanol at a temperature of 40-50°. The precipitate was separated by filtration, washed with aqueous alcohol, and dried at 100°. There was obtained 23.0 g (64.4%, calculated on the dihydrochloride) of the monosodium salt of tetraacetic acid 2,2'-diaminodiethyl ether.

Found %: N 7.79; Na 5.80. $C_{12}H_{19}O_9N_2Na$. Calculated %: N 7.82; Na 6.41.

SUMMARY

1. An improved method for the preparation of 2,2'-diaminodiethyl ether is described.

2. A method was developed for the preparation and separation of free tetraacetic acid 2,2'-diaminodiethyl ether and its monosodium salt.

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CONDENSATION OF 1-ALKOXYDIENES WITH ALDEHYDES

A NEW METHOD FOR THE SYNTHESIS OF α,β-UNSATURATED ALKOXYALDEHYDES AND POLYENE ALDEHYDES

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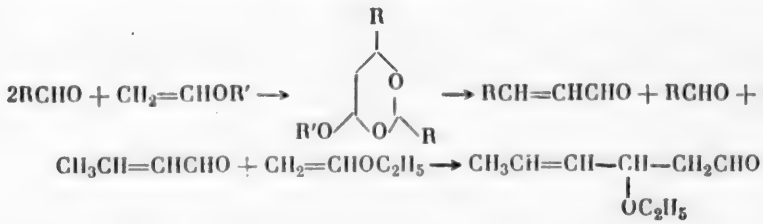
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3918-3926, December, 1960
Original article submitted January 13, 1960

The condensation of vinyl ethers with different saturated aldehydes [1, 2], which is one of the new methods for the synthesis of unsaturated aldehydes, is undoubtedly of interest. The reaction results in the formation of derivatives of 1,3-dioxane, which without being isolated, undergo hydrolysis of α, β-unsaturated aldehydes.



$$2RCHO + CH_2{=}CHOR' \longrightarrow \text{(1,3-dioxane)} \longrightarrow RCH{=}CHCHO + RCHO + R'OH$$

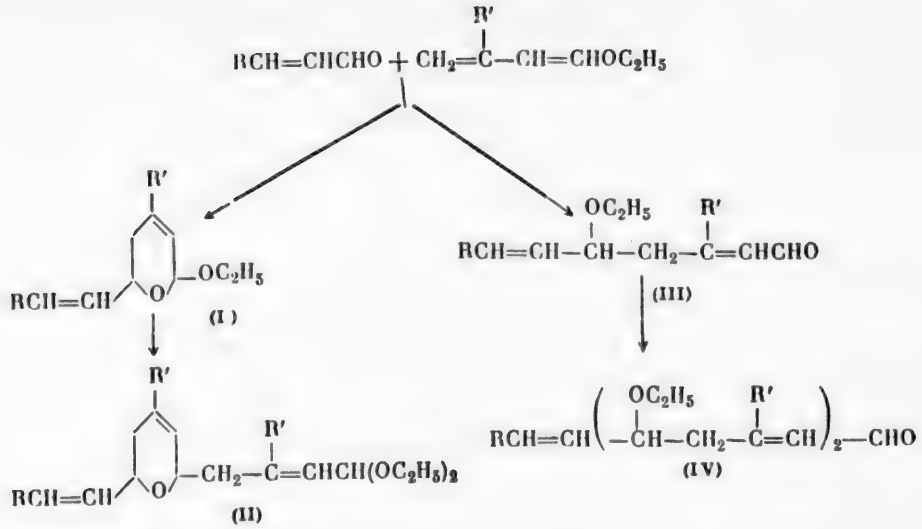
$$CH_3CH{=}CHCHO + CH_2{=}CHOC_2H_5 \longrightarrow CH_3CH{=}CH{-}CH(OC_2H_5){-}CH_2CHO$$

In one investigation devoted to a study of this method [3], it was shown that the reaction of aldehydes with vinyl ethers depends to a great extent on the nature of the catalyst and the structure of the original aldehyde. It was found that in a number of cases, not only derivatives of 1,3-dioxane, but also linear alkoxyaldehydes could be formed as a major reaction product; thus, for example, the condensation of crotonaldehyde with vinyl ethyl ether gives a 46% yield of 3-ethoxy-4 hexenal. No data on the condensation of aldehydes with dienic ethers has appeared in the literature to the present time.

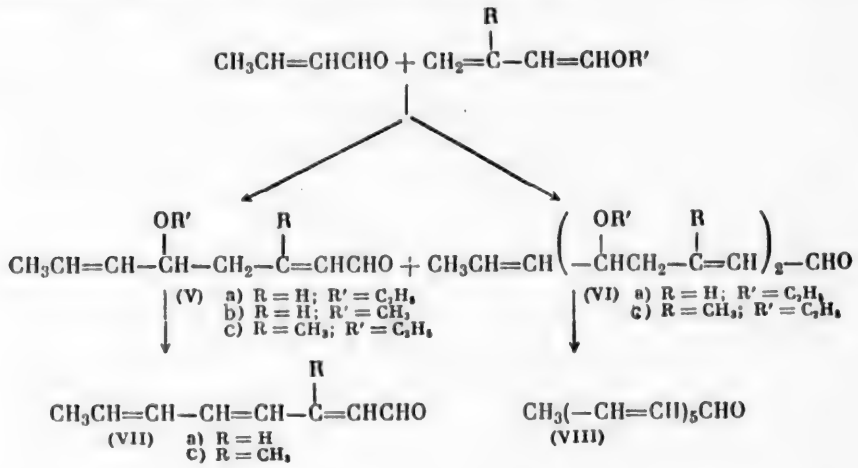
All of this undoubtedly lends interest to the study of the condensation of different aldehydes with 1-alkoxydienes, since, as has previously been shown, such dienic ethers behave in a manner similar to vinyl ethers in reactions with acetals of various unsaturated aldehydes [4].

With this aim, we carried out a detailed study of the condensation of 1-ethoxybutadiene and 1-ethoxyisoprene with various aldehydes. It was found that in the case of unsaturated aldehydes, the reaction with alkoxydienes takes place readily in the presence of such catalysts as BF_3, $ZnCl_2$, and $H_3BO_3 + (COOH)_2$ and leads to a mixture of products which can easily be separated by vacuum distillation.

It might be assumed that this reaction takes place as a result of 1,4-addition of the 1-alkoxydiene molecule across the C = O bond of the aldehyde with the initial formation of a derivative of dihydropyran (I), which as a cyclic hemiacetal, is able to react with a second molecule of diene giving the corresponding unsaturated acetal (II). However, a detailed study of the reaction products showed that they do not have this structure, but are the corresponding α, β-unsaturated alkoxyaldehydes (III) and (IV), the structures of which correspond to the addition of one or two molecules of 1-alkoxydiene to one molecule of aldehyde.



Thus, the condensation of crotonaldehyde with 1-ethoxybutadiene in the presence of boron trifluoride etherate gave 42 and 21% yields,* respectively, of alkoxyaldehydes (Va) and (VIa), which proved to be identical in physical constants and u.v. spectra to the alkoxyaldehydes previously obtained by saponification of the corresponding alkoxyacetals formed as a result of the condensation of crotonaldehyde acetal with 1-ethoxybutadiene [4]. Ethoxyaldehyde (Va) gives a 2,4-dinitrophenylhydrazone identical to that described previously, and it condenses with 1-ethoxybutadiene to give a 20% yield of diethoxyaldehyde (VIa).

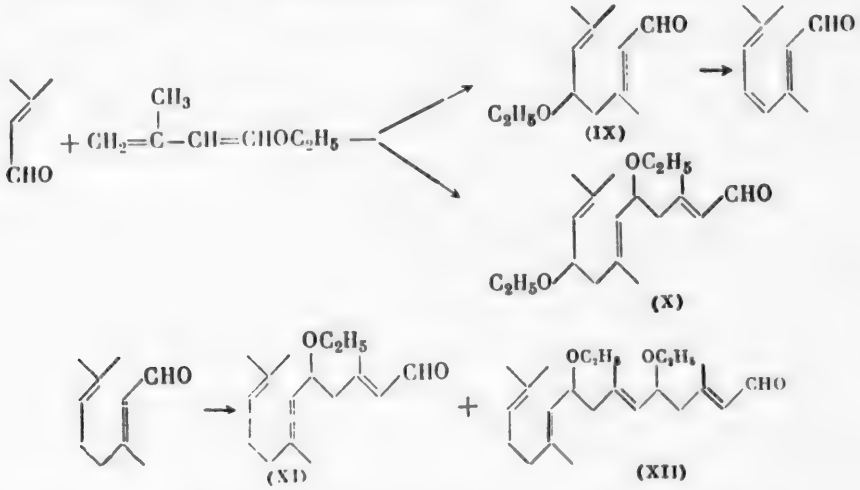


The condensation of crotonaldehyde proceeds in a similar manner with 1-methoxybutadiene and 1-ethoxyisoprene with the formation of δ-ethoxyaldehydes (Vb), (Vc), and (VIc). It is interesting that during the reaction of 2,4-dinitrophenylhydrazine with 3-methyl-5-ethoxy-2,6-octadienal (Vc), an alcohol is readily eliminated with the formation of the known 2,4-dinitrophenylhydrazone of 3-methyl-2,4,6-octatrienal (VIIc). Ethoxyaldehydes are also readily converted to the corresponding polyene aldehydes when heated with phosphoric acid, and 2,4,6-octatrienal (VIIa), 3-methyl-2,4,6-octatrienal (VIIc), and 2,4,6,8,10-dodecapentaenal (VIII) were prepared in good yields by this route.

A mixture of boric and oxalic acids proved to be the most satisfactory catalyst for the condensation of dimethylacrylaldehyde with ethoxyisoprene. In the presence of this catalyst, the reaction took place even at room temperature with the formation of a mixture of 5-ethoxycitral (IX) and 5,9-diethoxyfarnesal (X). These aldehydes, which were easily separable by vacuum distillation, were formed in yields of 45 and 17%, respectively. Both of

*In all cases, yields are based on the 1-alkoxydiene.

these ethoxyaldehydes absorb in the ultraviolet, and the wavelengths correspond to the presence of a double bond conjugated with the aldehyde group [5]. Ethoxyaldehyde (IX) readily formed a 2,4-dinitrophenylhydrazone, which was identical with dehydrocitral 2, 4-dinitrophenylhydrazone.



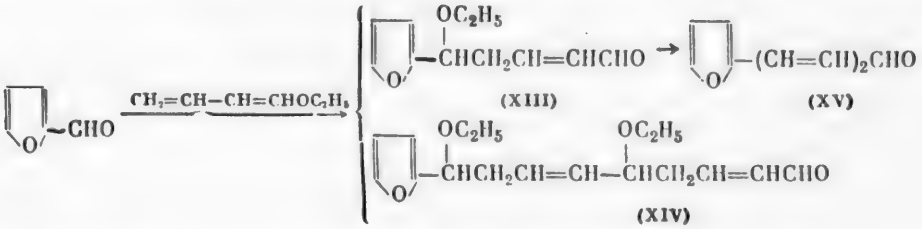
The condensation of citral with ethoxyisoprene may best be carried out in the presence of boron trifluoride etherate, and it gives a mixture of 5-ethoxyfarnesal (XI) and diethoxyaldehyde (XII) in yields of 28 and 29%, respectively. The structures of these ethoxyaldehydes were also confirmed by u.v. spectroscopy.

β-Cyclocitral and dihydro-o-tolualdehyde proved to be incapable of entering into condensation with 1-ethoxydienes. They also did not react with saturated aldehydes. In the presence of BF_3, butyraldehyde and isovaleraldehyde yield only polymeric products (apparently dimers and trimers), which, upon distillation with iodine, were converted to the original aldehydes.

Benzaldehyde condenses with ethoxybutadiene only with considerable difficulty, and 5-phenyl-5-ethoxy-2-pentenal is obtained in a yield of about 10% in this reaction.

In contrast to benzaldehyde, furaldehyde readily condenses with 1-ethoxybutadiene in the presence of boron trifluoride etherate or a mixture of boric and oxalic acids giving 5-furyl-5-ethoxy-2-pentenal (XIII) and 9-furyl-5,9-diethoxy-2 6 nonadienal (XIV), the structures of which were confirmed by u.v. spectroscopy.

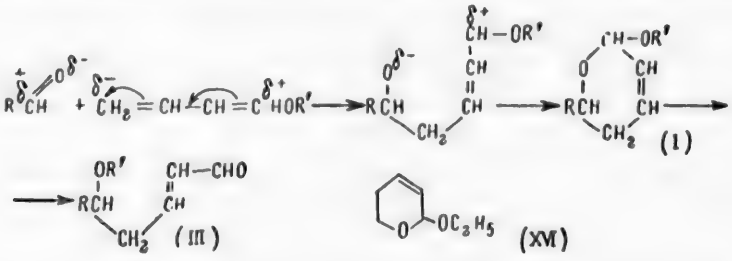
5-Furyl-5-ethoxy-2-pentenal (XIII) gave a 2,4-dinitrophenylhydrazone with a melting point which agreed with that reported in the literature [6]. Upon heating with dilute orthophosphoric acid, ethoxyaldehyde (XIII) readily lost a molecule of alcohol, being converted in good yield to the known 5-furyl-2,4 pentadienal (XV) [7].



Thus, this condensation of unsaturated aldehydes with 1-alkoxydienes provides a new and simple method for the synthesis of α,β-unsaturated alkoxyaldehydes. In a number of cases, the yields of reaction products are not lower than those obtained by the previously described method [4], which is based on the condensation of alkoxydienes with aldehyde acetals. All of this makes the new preparative method more convenient for the synthesis of various polyene aldehydes, since conversion of the original aldehyde to the acetal is avoided, and the α,β-unsaturated alkoxyaldehydes are formed immediately.

As an explanation of the mechanism of the formation of δ-alkoxyaldehydes during the condensation of unsaturated aldehydes with 1-alkoxydienes, it could be proposed that this reaction proceeds through dihydropyran (I), in which disproportionation of the alkoxyl group takes place leading to the formation of the corresponding alkoxyaldehyde (III).

Such disproportionation of dihydropyran (I) would have to take place very readily, since only in such a case is it possible to explain the formation of alkoxyaldehyde (IV), rather than its acetal, as a secondary reaction product.



However, we were unable to confirm that the alkoxyl group disproportionates readily, since 2-ethoxy-5,6-dihydropyran (XVI), which was prepared by a known method [8], proved to be quite stable and incapable of undergoing change under the influence of boron trifluoride etherate or a mixture of boric and oxalic acids.

Thus, the formation of δ-alkoxyaldehydes through the intermediate dihydropyran (I) is not very likely, although the possibility cannot be completely excluded.

Apparently, the formation of δ-alkoxyaldehydes during the condensation of aldehydes with 1-alkoxydienes proceeds by the scheme proposed in the literature [3] for the condensation of aldehydes with vinyl ethers; however, confirmation of this mechanism requires additional investigation.

EXPERIMENTAL*

Condensation of Crotonaldehyde with 1-Ethoxybutadiene

To 16 g of crotonaldehyde, cooled to 0°, were added, with stirring, 0.05 g of boron trifluoride etherate in 4 ml of absolute ether and 11.2 g of 1-ethoxybutadiene; the additions were made from two funnels in a stream of nitrogen over a period of 40 min. Halfway through the addition of the catalyst, the temperature rose to 25°, and it was then quickly lowered to + 3°. The reaction mixture was stirred for 4 hr at 3-10°, and was then neutralized with sodium ethylate and distilled. The following substances were obtained: 1) 9 g of the original crotonaldehyde with a b.p. of 100-104°; 2) 6.7 g of 5-ethoxy-2,6-octadienal (Va).

B.p. 60-63° (0.05 mm), 111-113° (16 mm), $n^{20}D$ 1.4665, d^{20}_4 0.9251. λ_{max} (in ethanol) 223 mμ (log ε 4.091), 295.5 mμ (log ε 2.554).

Found %: C 71.10, 71.21; H 9.56, 9.48. $C_{10}H_{16}O_2$. Calculated %: C 71.41; H 9.59.

The 2,4-dinitrophenylhydrazone of aldehyde (Va) had an m.p. of 138-140° (from ethanol), and a mixture of it with the 2,4-dinitrophenylhydrazone of aldehyde (Va) prepared from 1,1,5-triethoxy-2,6-octadiene [4] showed no depression of the melting point.

λ_{max} (in heptane) 249 mμ (log ε 4.124), 358 mμ (log ε 4.407).

Found %: C 55.11, 55.14; H 5.96, 5.83; N 16.26, 16.40. $C_{16}H_{20}O_5N_4$. Calculated %: C 55.11; H 5.77; N 16.08.

3) 5,9-Diethoxy-2,6,10-dodecatrienal (VIa), 3.2 g.

B.p. 95-99° (0.08 mm), $n^{20}D$ 1.4775, d^{20}_4 0.9550, λ_{max} (in ethanol) 222.5 mμ (log ε 4.178), 273 mμ (log ε 2.431).

Found %: C 71.60, 71.46; H 9.73, 9.45. $C_{16}H_{26}O_3$. Calculated %: C 72.13; H 9.83.

*The u.v. spectra were taken by T. M. Fadeeva.

4) Residue, 7.5 g.

Condensation of 5-ethoxy-2,6 octadienal (Va) with 1-ethoxybutadiene. From 9 g of 5-ethoxy 2,6 octadienal (Va), 2.7 g of 1 ethoxybutadiene, and 0.025 g of boron trifluoride etherate was obtained, by the method described above, 1.4 g of 5,9-diethoxy-2,6,10-dodecatrienal (VIa); 6.1 g of the original aldehyde (Va) was recovered.

2,4,6-Octatrienal (VIIa). A mixture of 4 g of 5-ethoxy-2,6-octadienal (Va), 4 ml of 85% orthophosphoric acid, and 20 ml of water was heated in a stream of nitrogen and with stirring on a boiling water bath for 40 min. The reaction mixture was cooled, and ether was added. The ether layer was separated, and the aqueous layer was extracted with ether. The combined ether extracts were washed with a solution of sodium bicarbonate and with water, dried with calcined magnesium sulfate, and distilled in a stream of nitrogen. There was obtained 2.6 g of 2,4,6-octatrienal (VIIa) with a b.p. of 44-45° (0.3 mm), which, upon cooling, crystallized as a cream-colored mass. After two recrystallizations from petroleum ether, the material melted at 57-58°. A mixture with (VIIa) prepared by polyene condensation of crotonaldehyde [9] melted at 56-58°.

2,4,6,8,10-Dodecapentaenal (VIII). A mixture of 2.2 g of 5,9-diethoxy-2,6,10-dodecatrienal (VIa), 2 ml of 85% orthophosphoric acid, and 10 ml of water was heated in a stream of nitrogen and with stirring at 90° for 40 min. The reaction mixture was then subjected to the treatment described above. After distillation of the ether, the residue (1.5 g) crystallized; two recrystallizations from methanol yielded 2,4,6,8,10-dodecapentaenal (VIII) with an m.p. of 157-159°. A mixture of (VIII) with a sample of 2,4,5,8,10-dodecapentaenal prepared earlier [9] melted at 157-160°.

Condensation of Crotonaldehyde with Methoxybutadiene

From 9 g of crotonaldehyde, 4.3 g of 1-methoxybutadiene, and 0.025 g of boron trifluoride etherate in 4 ml of absolute ether was obtained, by the method described above, 3.2 g of 5-methoxy-2,6-octadienal (Vb).

B.p. 43-45° (0.08 mm), 109-113° (17 mm), $n^{20}D$ 1.4740, d^{20}_4 0.9406.

Found %: C 69.52, 69.52; H 8.98, 9.03. $C_9H_{14}O_2$. Calculated %: C 70.09; H 9.14.

The 2,4-dinitrophenylhydrazone of aldehyde (Vb) melted at 120-122° (from ethanol).

λ_{max} (in isooctane) 358 mμ.

Found %: N 16.65, 16.86. $C_{15}H_{18}O_5N_4$. Calculated %: N 16.76.

Condensation of Crotonaldehyde with Ethoxyisoprene

a) To 40 g of crotonaldehyde, precooled to −5°, were added 21.4 g of ethoxyisoprene and 0.05 g of boron trifluoride etherate in 12 ml of absolute ether; the addition was carried out over a period of 2 hr with continuous stirring and in a stream of nitrogen. The temperature rose to 20° halfway through the addition, and it was quickly lowered. After the addition of the ethoxyisoprene, the reaction mixture was stirred for 1.5 hr at a temperature of −5 to 0°, and was then neutralized with sodium ethylate. The ether and the crotonaldehyde were distilled, and the residue was distilled under vacuum. The following substances were obtained:

1) 3-Methyl-5-ethoxy-2,6-octadienal (Vc), 7.5 g.

B.p. 61-62° (0.4 mm), $n^{20}D$ 1.4728, d^{20}_4 0.9311. λ_{max} (in ethanol) 239.5 mμ (log ε 4.073), 320.5 mμ (log ε 2.672).

Found %: C 71.99, 71.84; H 10.00, 9.96. $C_{11}H_{18}O_2$. Calculated %: C 72.46; H 9.95.

The reaction of aldehyde (Vc) with an aqueous methanol solution of 2,4-dinitrophenylhydrazine gave the 2,4-dinitrophenylhydrazone of 3-methyl-2,4,6-octatrienal (VIIc) with an m.p. of 190-192° (from ethyl acetate), which is in agreement with the literature value [10].

2) 3,7-Dimethyl-5,9-diethoxy-2,6,10-dodecatrienal (VIc), 3.5 g.

B.p. 114-117° (0.25 mm), $n^{20}D$ 1.4903, d^{20}_4 0.9539, λ_{max} (in ethanol) 240 mμ (log ε 4.1662), 334.5 mμ (log ε 2.866).

Found %: C 72.85; 72.78, H 10.04; 9.97. $C_{18}H_{30}O_3$. Calculated %: C 73.45; H 10.28.

b) To 18.5 g of crotonaldehyde containing 0.015 g of H_3BO_3 + $(COOH)_2$ catalyst [3] was added, with stirring, 9 g of ethoxyisoprene; the addition was carried out over a period of 1 hr. The reaction temperature increased from 22 to 29° during the addition. After the ethoxyisoprene had been added, the reaction mixture was stirred for 1 hr at room temperature and for 15 min at 40°; it was then diluted with ether and neutralized with 0.2 g of sodium carbonate in 7 ml of water. The ether solution was washed with water, dried with calcined magnesium sulfate, and distilled. There were obtained 3.5 g of aldehyde (Vc) with an b.p. of 59-62° (0.5 mm) and 2.4 g of aldehyde (VIc) with a b.p. of 115-118° (0.1 mm).

3-Methyl-2,4,6-octatrienal (VIIc). A mixture of 2.4 g of 3-methyl-5-ethoxy-2,6-octadienal (Vc), 2.4 ml of 85% orthophosphoric acid, and 12 ml of water was stirred in a stream of nitrogen at 90° for 40 min. The usual treatment gave 1.4 g of 3-methyl-2,4,6-octatrienal (VIIc) with a b.p. of 58-60° (0.25 mm), $n^{20}D$ 1.5695.

The 2,4-dinitrophenylhydrazone of aldehyde (VIIc) melted at 191-192° (from ethyl acetate). The semicarbazone of aldehyde (VIIc) melted at 182-183° (from 65% aqueous methanol). According to the literature, the 2,4-dinitrophenylhydrazone of aldehyde (VIIc) melts at 192-193°, and the semicarbazone melts at 179° [10].

Condensation of Dimethylacrylaldehyde with Ethoxyisoprene

To 15.6 g of dimethylacrylaldehyde containing 0.015 g of catalyst (boric acid + oxalic acid) was added 8.5 g of ethoxyisoprene; the temperature of the reaction mixture rose from 29 to 34° over the 40 min period of addition. The mixture was then stirred for 30 min at room temperature and for 10 min at 10°. The usual treatment followed by distillation gave the following substances:

1) The original dimethylacrylaldehyde, 9.8 g, b.p. 62-66° (55 mm), $n^{20}D$ 1.4600.

2) 3,7-Dimethyl-5-ethoxy-2,6-octadienal (IX), 6.6 g.

B.p. 59-61° (0.06 mm), $n^{20}D$ 1.4780, λ_{max} (in ethanol) 240 mμ (log ε 4.164), 330.5 mμ (log ε 2.117).

The reaction of aldehyde (IX) with a hydrochloric acid solution of 2,4-dinitrophenylhydrazine gave the 2,4-dinitrophenylhydrazone of dehydrocitral; m.p. 210-212° (from a mixture of ethanol and ethyl acetate). A mixture of this material with the 2,4-dinitrophenylhydrazone of dehydrocitral prepared by polyene condensation of dimethylacrylaldehyde [9] melted at 210-212°.

3) 3,7,11-Trimethyl-5,9-diethoxy-2,6,10-dodecatrienal (X), 2.2 g.

B.p. 107-108° (0.05 mm), $n^{20}D$ 1.4880, λ_{max} (in ethanol) 240 mμ (log ε 4.164), 335.5 mμ (log ε 2.841).

Condensation of Citral with Ethoxyisoprene

The citral, 14.3 g was cooled with ice water, and 4.5 g of ethoxyisoprene and 0.05 g of boron trifluoride etherate in 4 ml of absolute ether were simultaneously added with stirring. The reaction mixture was allowed to stand for 1 hr, and was then subjected to the usual treatment. The following substances were isolated by distillation:

1) Citral, 10.5 g, b.p. 63-67° (0.1 mm), $n^{19.5}D$ 1.4870.

2) 3,7,11-Trimethyl-5-ethoxy-2,6,10-dodecatrienal (XI), 3 g.

B.p. 103-106° (0.08 mm), $n^{19.5}D$ 1.4900, λ_{max} (in ethanol) 239 mμ (log ε 4.089), 338 mμ (log ε 3.006).

Found %: C 77.40, 77.46; H 10.78, 10.81. $C_{17}H_{28}O_2$. Calculated %: C 77.21; H 10.67.

3) 3,7,11,15-Tetramethyl-5,9-diethoxy-2,6,10,14-eicosatetraenal (XII), 2.2 g.

B.p. 140-143° (0.05 mm), $n^{20}D$ 1.5020, λ_{max} (in ethanol) 239.5 mμ (log ε 4.160), 338 mμ (log ε 3.484).

Condensation of Benzaldehyde with Ethoxyisoprene

The benzaldehyde, 19.5 g, was cooled with ice water, and 9 g of ethoxybutadiene and 0.05 g of boron trifluoride etherate in 5 ml of absolute ether were simultaneously added with stirring. After the usual treatment, the benzaldehyde (17 g, b.p. 70-75° at 15 mm) was removed by distillation, and two subsequent distillations gave 1.7 g of 5-phenyl-5-ethoxy-2-pentenal.

B.p. 84-86° (0.06 mm), $n^{20}D$ 1.5197, λ_{max} (in ethanol) 218 mμ (log ε 4.188).

The 2,4-dinitrophenylhydrazone of 5-phenyl-5-ethoxy-2-pentenal melted at 154-155° (from a mixture of ethanol and ethyl acetate).

λ_{max} (in heptane) 358 mμ.

Found %: N 14.35, 14.60. $C_{19}H_{20}O_5N_4$. Calculated %: N 14.57.

The undistillable residue amounted to 8 g.

Condensation of 2-Furaldehyde with Ethoxybutadiene

To 25 g of 2-furaldehyde containing 0.022 g of the catalyst, H_3BO_3 + $(COOH)_2$, was added 10 g of ethoxybutadiene; the addition was carried out over a period of 40 min with continuous stirring. The temperature of the reaction mixture rose from 18 to 33° during the addition. The reaction mixture was allowed to stand for 1 hr at room temperature, and was then treated with 0.3 g of sodium carbonate in 10 ml of water. The lower layer was washed with water, and the upper layer was extracted with ether. The lower layer and the ether extract were combined, dried with calcined magnesium sulfate, and distilled. The following substances were obtained:

1) 2-Furaldehyde, 16.7 g, b.p. 60-63° (15 mm), $n^{20}D$ 1.5220.

2) 5-Furyl-5-ethoxy-2-pentenal (XIII), 4.0 g.

B.p. 80-81° (0.07 mm), $n^{20}D$ 1.4928, d^{20}_4 1.043, λ_{max} (in ethanol) 219 mμ (log ε 4.342), 347.5 mμ (log ε 2.124).

Found %: C 67.85, 67.74; H 7.23, 7.28. $C_{11}H_{14}O_3$. Calculated %: C 68.04; H 7.27.

The 2,4-dinitrophenylhydrazone of aldehyde (XIII) melted at 142-144° (from a mixture of ethanol and ethyl acetate); this is in agreement with the literature value [6].

3) 9-Furyl-5,9-diethoxy-2,6-nonadienal (XIV), 2.8 g.

B.p. 120-122° (0.07 mm), $n^{20}D$ 1.4928, d^{20}_4 1.016, λ_{max} (in ethanol) 219 mμ (log ε 4.415), 315 mμ (log ε 2.487).

Found %: C 39.90, 69.90; H 8.20, 8.16. $C_{17}H_{24}O_4$. Calculated %: C 69.83; H 8.27.

The undistillable residue amounted to 5.8 g.

5-Furyl-2,4-pentadienal (XV). A mixture of 4 g of furyl-5-ethoxy-2-pentenal (XIII), 4 ml of 85% orthophosphoric acid, and 20 ml of water was stirred in a stream of nitrogen on a boiling water bath for 5 min. After the usual treatment, the products were distilled under vacuum in a stream of nitrogen containing traces of hydroquinone. There was obtained 1.8 g of 5-furyl-2,4-pentadienal (XV) with a b.p. of 73-76° (0.06 mm); this material crystallized during distillation to a yellow mass. The m.p. of (XV) was 65-66° (from ethanol), which is in agreement with the literature value [7].

SUMMARY

A new method is presented for the preparation of δ-alkoxyaldehydes and polyene aldehydes. The method is based on the condensation of 1-alkoxydienes with α,β-unsaturated aldehydes.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

ESTERS OF 1,3-DIMETHYL-
AND 1,2,3-TRIMETHYL-4-CARBOMETHOXY-4-PIPERIDOLS

NEW ANALOGS OF α-COCAINE AND α-EUCAINE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3926-3931, December, 1960
Original article submitted January 8, 1960

One of the simplest and most practicable methods for the synthesis of γ-piperidones with different substituents in the piperidone ring is the interaction of divinyl ketones and the corresponding methoxy derivatives with ammonia and primary amines [1]. Another original method for the synthesis of γ-piperidones has recently been developed [2]. This method is based on vinylacetylenic hydrocarbons (enynes), and makes use of aminomethylation.

In accordance with the proposal of I. N Nazarov, the author of the methods mentioned above, in our earlier work [3] we undertook the synthesis of new anesthetics and analgesics starting with 1,3-dimethyl- and 1,2,3-trimethyl-4-piperidones, which are easily obtained by the second method. In recent years, derivatives of 1,3-dimethyl-4-piperidone have attracted the attention of investigators in connection with the high analgesic activity possessed by propionic esters of the stereoisomeric 1,3-dimethyl-4-phenyl-4-piperidols, one of which – Nisentil (β-prodine) [5] – has found clinical application.

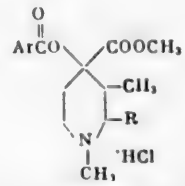
The present communication described some esters of 1,3-dimethyl- and 1,2,3-trimethyl-4-carbomethoxy-4-piperidols which are structurally similar to α-cocaine [6] and analogous to α-eucaine [7].

1,3-Dimethyl-4-piperidone and 1,2,3-trimethyl-4-piperidone were easily converted to the corresponding cyanohydrins – 1,3-dimethyl-4-cyano-4-piperidol (I) and 1,2,3-trimethyl-4-cyano-4-piperidol (II) – by an exchange reaction with acetonecyanohydrin according to a known method [8].

The nucleophilic addition of hydrogen cyanide to the carbonyl group of piperidones takes the same steric course as previously demonstrated by us for 1-alkyl-2,5-dimethyl-4-piperidones [9], and it leads to the formation of only one of two stereoisomeric cyanohydrins corresponding to 1,3-dimethyl-4-piperidone and to one of the four diastereoisomeric racemic cyanohydrins possible for 1,2,3-trimethyl-4-piperidone.

Concentrated hydrochloric acid readily saponified cyanohydrin (I) to the hydroxy acid (III), which was separated as the hydrochloride. This is in contrast to cyanohydrin (II), which decomposed to a considerable extent under the same conditions, being converted to the original piperidone; the latter is formed as a result of cleavage of hydroxy acid (IV) in a manner similar to the decomposition previously observed for certain α-hydroxy acids on heating and under the influence of concentrated mineral acids [10]. Acid hydrolysis of cyanohydrin (II) in the cold (over a period of 3 days) leads to the same result. Esterification of hydroxy acids (III) and (IV) with methyl alcohol gave the corresponding hydroxy esters – 1,3-dimethyl-4-carbomethoxy-4-piperidol (V) and 1,2,3-trimethyl-4-carbomethoxy-4-piperidol (VI).

Esters of 1,3-Dimethyl- and 1,2,3-Trimethyl-4-carbomethoxy-4-piperidols

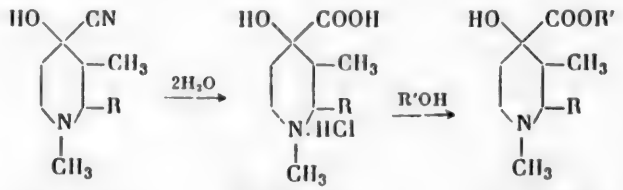


No. of comp. in text	R	Ar	Melting point	Solvent used for recrystallization	Yield (in %)	Empirical formula	% N	
							found	calc.
(X)	H	C_6H_5	189—190°	al+ac	95	$C_{16}H_{22}O_4NCl$	4.44, 4.55	4.27
(XI)	H	$C_6H_5CH_2$	165—166	b+al	91	$C_{17}H_{24}O_4NCl$	3.94, 4.30	2.09
(XII)	H	$C_6H_5OCH_2$	178—179	al	98	$C_{17}H_{24}O_5NCl$	4.19, 4.07	3.91
(XIII)	H	$(C_6H_5)_2CH$	163—164	b+al	83	$C_{23}H_{28}O_4NCl$	3.20, 3.23	3.35
(XIV)	H	$C_6H_5CH=CH$	219—220	al	95.5	$C_{18}H_{24}O_4NCl$	3.88, 3.97	3.96
(XV)	H	$C_6H_5OCH_2CH_2$	173—174	al	88.5	$C_{18}H_{26}O_5NCl$	3.79, 3.78	3.76
(XVI)	H	$p\text{-}NO_2C_6H_4$	195—196	al	96	$C_{16}H_{21}O_6N_2Cl$	7.48, 7.15	7.43
(XVII)	H	$C_6H_5CH_2CH_2$	202—203	ac+al	81.5	$C_{18}H_{26}O_4N_2Cl$	4.03, 4.36	3.93
(XVIII)	H	$p\text{-}NH_2C_6H_4$	219—220	ac+al	92.5	$C_{16}H_{23}O_4N_2Cl$	8.29, 8.17	8.08
(XIX)	CH_3	$C_6H_5OCH_2$	153—154	ea	90	$C_{18}H_{26}O_5NCl$	3.91, 3.81	3.77
(XX)	CH_3	$C_6H_5CH=CH$	207—208	ac	91	$C_{19}H_{26}O_4NCl$	4.07, 4.14	3.83
(XXI)	CH_3	$C_6H_5CH_2CH_2$	172—173	ac	85.6	$C_{19}H_{28}O_4NCl$	3.65, 3.61	3.79

Note. b – benzene, ac – acetone, al – alcohol, ea – ethyl acetate.

Alcoholysis of cyanohydrin (II) in the presence of concentrated sulfuric acid [11] did not increase the yield of hydroxy ester (VI), since under these conditions significant amounts of 1,2,3-trimethyl-4-piperidone are invariably formed.

Starting with hydroxy acid (III), we also obtained other 1,3-dimethyl-4-carbalkoxy-4-piperidols (VII-IX) in addition to hydroxy ester (V).



(I) R = H
(II) R = CH_3

(III) R = H
(IV) R = CH_3

(V) R = H, R' = CH_3
(VI) R = CH_3, R' = CH_3
(VII) R = H, R' = C_2H_5
(VIII) R = H, R' = C_3H_7
(IX) R = H, R' = C_4H_9

The interaction of 1,3-dimethyl-4-carbomethoxy-4-piperidol (V) with the chlorides of aromatic and arylaliphatic acids readily gave the hydrochlorides of the corresponding esters: benzoic (X), phenylacetic (XI), phenoxyacetic (XII), diphenylacetic (XIII), cinnamic (XIV), β-phenoxypropionic (XV), and p-nitrobenzoic (XVI). Hydrogenation of the hydrochlorides of the cinnamate (XIV) and the p-nitrobenzoate (XVI) in the presence of a skeletal nickel catalyst gave, respectively, the hydrochlorides of β-phenylpropionic (XVII) and p-aminobenzoic (XVIII) esters. The diphenylacetic ester (XIII) is of interest in view of its possible antispasmodic activity [12].

A similar route was used to prepare the hydrochlorides of three esters – phenoxyacetic (XIX), cinnamic (XX), and, by hydrogenation of the latter, β-phenylpropionic (XXI) – from 1,2,3-trimethyl-4-carbomethoxy-4-piperidol (VI). The selection of these compounds was based on the fact that among the similar esters described in one of our previous communications [13], it was precisely such esters which displayed maximum anesthetic activity, an activity close to that of dicaine for nerve blocking and infiltration anesthesia.

The properties of these new analogs of α-cocaine and α-eucaine – the esters of 1,3-dimethyl- and 1,2,3-trimethyl-4-piperidols (V) and (VI) – are shown in the table.

The interaction of 1,3-dimethyl-4-carbomethoxy-4-piperidol (V) with phenyllithium leads to the transformation of 1,3-dimethyl-4-hydroxy-4-piperidylphenylcarbinol (XXII), which, under the influence of a Lewis acid (anhydrous zinc chloride in acetic anhydride), undergoes a pinacoline-type dehydration and is converted to 1,3-dimethyl-4-phenyl-4-piperidyl phenyl ketone (XXIII), which is a close analog of ketobemidone (cliradon) [14], one of the strongest analgesics of the piperidine series.

EXPERIMENTAL

The original 1,3-dimethyl-4-piperidone and 1,2,3-trimethyl-4-piperidone were prepared by previously described methods [2], and the 1,3-dimethyl-4-piperidone used for comparison was prepared by another known method [4].

1,3-Dimethyl-4-cyano-4-piperidol (I). A mixture of 51.7 g of 1,3-dimethyl-4-piperidone and 44.8 g of acetonecyanohydrin (b.p. 65-67° at 7 mm) was prepared. The mixture was allowed to stand for a day, and the crystalline product was then separated by filtration and dried in a vacuum desiccator. There was obtained 48 g of cyanohydrin (I) with an m.p. of 90-92° (from petroleum ether). An additional 1.8 g of crystalline product with an m.p. of 88-90°, identical to the main product, was obtained from the filtrate. A total of 49.8 g (95.9%) of cyanohydrin (I) was obtained in this experiment.

Found %: N 18.19, 18.40. $C_8H_{14}ON_2$. Calculated %: N 18.23.

1,3-Dimethyl-4-hydroxy-4-piperidylcarboxylic acid hydrochloride (III). A mixture of 17 g of 1,3-dimethyl-4-cyano-4-piperidol (I) and 60 ml of concentrated hydrochloric acid was heated for 8 hr on a boiling water bath. After removal of the hydrochloric acid under vacuum, the solid residue was dissolved in a 30% aqueous solution of sodium hydroxide and heated for 3 hr until the evolution of ammonia ceased. The reaction mixture was evaporated under vacuum to half its volume, made acid (to Congo indicator) with concentrated hydrochloric acid, and, after removal of the excess hydrochloric acid under vacuum, it was freed of traces of water by azeotropic distillation with benzene and extracted with 100 ml of anhydrous alcohol. The addition of absolute ether to the alcohol extract caused separation of 15.6 g (65%) of the hydrochloride of hydroxy acid (IV). This material was in the form of prismatic crystals with an m.p. of 192-193° (from anhydrous alcohol).

Found %: C 45.47; 45.54; H 7.57, 7.39; N 6.48, 6.70. $C_8H_{16}O_3NCl$. Calculated %: C 45.82; H 7.63, N 6.67.

1,3-Dimethyl-4-carbomethoxy-4-piperidol (V). 1,3-Dimethyl-4-hydroxy-4-piperidinecarboxylic acid (III) hydrochloride, obtained by saponification of 49.5 g of cyanohydrin (I) as described above, was esterified by heating with 150 ml of anhydrous methyl alcohol at 70-80° for 4 hr, during which time dry hydrogen chloride was continuously passed into the solution. After removal of the methanol, the residue was dissolved in 80 ml of water and treated with potassium carbonate. The oily base was extracted with 300 ml of ether, and the extract was dried with calcined magnesium sulfate. After evaporation of the solvent, distillation of the residue under vacuum gave the following fractions: first fraction, b.p. 65-67° (8 mm), 7.2 g; second fraction, b.p. 108-110° (8 mm), 36.8 g. The first fraction – 1,3-dimethyl-4-piperidone – was formed as a result of partial decomposition of cyanohydrin (I). The second fraction crystallized completely. There was obtained 35.6 g (53.7%) of hydroxy ester (V) with an m.p. of 57-58° (from petroleum ether).

Found %: C 57.67, 57.99; H 9.25, 9.14; N 7.26, 7.36. $C_9H_7O_3N$. Calculated %: C 57.75; H 9.09; N 7.46.

1,3-Dimethyl-4-carbethoxy-4-piperidol (VII). The hydrochloride of hydroxy acid (III) (5.3 g) was esterified with 50 ml of anhydrous alcohol, as described above. The usual treatment resulted in 4 g (76%) of hydroxy ester (VII).

B.p. 99-101° (1.5 mm), d^{20}_4 1.062, $n^{20}D$ 1.4742, MR 53.22; calc. 53.30.

Found %: N 6.60, 6.69. $C_{10}H_{19}O_3N$. Calculated %: N 6.96.

The hydrochloride melted at 148-150° (from acetone).

Found %: N 5.73; 5.67. $C_{10}H_{20}O_3NCl$. Calculated %: N 5.80.

1,3-Dimethyl-4-carbopropoxy-4-piperidol (VIII). Hydrochloride of hydroxy acid (III) was prepared by saponification of 10 g of cyanohydrin (I), and, without separation from the ammonium chloride, it was esterified by heating with 100 ml of anhydrous propyl alcohol at 130-136° for 3.5 hr, during which time hydrogen chloride was continuously passed through the reaction mixture. The usual treatment resulted in 9.5 g (68%) of hydroxy ester (VIII).

B.p. 110-112° (1 mm), d^{20}_4 1.0400, $n^{20}D$ 1.4739, MR 58.08; calc. 58.06.

Found %: C 61.64, 61.56; H 9.72, 9.50; N 6.80, 6.56. $C_{11}H_{21}O_3N$. Calculated %: C 61.32; H 9.76; N 6.51.

The hydrochloride melted at 126-128° (from acetone).

Found %: N 5.54, 5.34. $C_{11}H_{22}O_3NCl$. Calculated %: N 5.57.

1,3-Dimethyl-4-carbobutoxy-4-piperidol (IX). The hydrochloride of hydroxy acid (III), obtained by saponification of 7 g of cyanohydrin (I), was similarly esterified by heating with 90 ml of n-butyl alcohol at 130-140° for 3.5 hr. The usual treatment gave 7.3 g (70%) of hydroxy ester (IX).

B.p. 128-130° (2 mm), d^{20}_4 1.024, $n^{20}D$ 1.4730, MR 62.69; calc. 62.43.

Founf %: N 6.08, 6.13. $C_{12}H_{23}O_3N$. Calculated %: N 6.11.

The hydrochloride melted at 120-122° (from acetone).

Found %: N 5.33, 5.07. $C_{12}H_{24}O_3NCl$. Calculated %: N 5.27.

1,2,3-Trimethyl-4-cyano-4-piperidol (II). A mixture of 47.8 g of 1,2,3-trimethyl-4-piperidone and 29.9 g of acetonecyanohydrin was allowed to stand for a day, and at the end of this time it was found to be completely crystallized. There was obtained 51.5 g (90.5%) of cyanohydrin (II); the colorless crystals had an m.p. of 95-96° (from ethyl acetate).

Found %: N 16.41; 16.53. $C_9H_{16}ON_2$. Calculated %: N 16.67.

1,2,3-Trimethyl-4-carbomethoxy-4-piperidol (VI). Saponification of 51.5 g of 1,2,3-trimethyl-4-cyano-4-piperidol (II) was carried out by heating with 200 ml of concentrated hydrochloric acid on a boiling water bath for 5 hr. The reaction mixture was cooled, the precipitated ammonium chloride was removed by filtration, and the filtrate was evaporated to dryness under vacuum. The resulting hydrochloride of hydroxy acid (IV) was not separated, but was esterified in the reaction mixture with 400 ml of anhydrous methanol as described above for the esterification of hydroxy acid (V). After the usual treatment, two fractions were obtained by vacuum distillation: first fraction, b.p. 68-70° (7 mm), 21 g; second fraction, b.p. 105-107° (3 mm), 19.8 g. The first fraction was 1,2,3-trimethyl-4-piperidone formed by decomposition of cyanohydrin (II). The second fraction crystallized completely. There was obtained 19.8 g (32.5%) of hydroxy ester (VI); the lustrous colorless prisms melted at 125-126° (from acetone).

Found %: N 7.24, 7.14, $C_{10}H_{19}O_3N$. Calculated %: N 6.96.

Benzoic ester of 1,3-dimethyl-4-carbomethoxy-4-piperidol (X). A solution of 3 g of 1,3-dimethyl-4-carbomethoxy-4-piperidol (V) in 10 ml of anhydrous benzene was mixed with 6.6 g of benzoyl chloride and heated for 3.5 hr on a boiling water bath. The reaction mixture was washed with anhydrous ether to the disappearance of the odor of the acid chloride and ground to a powder under ether. The powder was separated by filtration and recrystallized from a mixture of acetone and anhydrous alcohol. There was obtained 5 g (95%) of the benzoate of (X) in the form of snow-white crystals (see table).

Other esters of 1,3-dimethyl-4-carbomethoxy-4-piperidol (V) and 1,2,3-trimethyl-4-carbomethoxy-4-piperidol (VI) were prepared by a similar method. The properties of these compounds are reported in the table.

1,3-Dimethyl-4-hydroxy-4-piperidyldiphenylcarbinol. To a solution of phenyllithium, prepared from 3 g of lithium and 28.2 g of bromobenzene in 60 ml of absolute ether, was added 9.8 g of 1,3-dimethyl-4-carbomethoxy-4-piperidol (V); the addition was carried out over a period of 1 hr. The reaction mixture was heated for 4 hr at the boiling point of ether, and was then hydrolyzed with 100 ml of 18% hydrochloric acid. The ether layer was separated, and the aqueous layer was concentrated under vacuum. There was obtained 12.9 g (79%) of the glycol hydrochloride; the colorless crystals melted at 259 259.5° (from acetone).

Found %: N 4.42, 4.34. $C_{20}H_{26}O_2NCl$. Calculated %: N 4.53.

1,3-Dimethyl-4-phenyl-4-piperidyl phenyl ketone. A mixture of 11 g of 1,3-dimethyl-4-hydroxy-4-piperidyldiphenylcarbinol hydrochloride, 9 g of finely powdered anhydrous zinc chloride, and 37 ml of acetic anhydride was heated for 4 hr on a boiling water bath. The mixture was then diluted with 50 ml of water, neutralized with potassium carbonate, and extracted five times with ether (250 ml). The ether extracts were combined and dried with calcined magnesium sulfate. The solvent was evaporated, and 6.6 g (71.5%) of the ketone was obtained; the colorless prisms melted at 118.5-120° (from ligroin with a boiling range of 80-100°).

Found %: N 4.83, 5.03. $C_{20}H_{23}ON$. Calculated %: N 4.77.

SUMMARY

The cyanohydrins of 1,3-dimethyl- and 1,2,3-trimethyl-4-piperidones were utilized as starting points for the synthesis of the corresponding 4-carbomethoxy-4-piperidols and their esters, which are new analogs of α-cocaine and α-eucaine.

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AN INVESTIGATION OF THE PROPERTIES OF AMINO ACIDS AND PEPTIDES CONTAINING A TERTIARY NITROGEN ATOM

V. THE EFFECT OF DIBENZYL PROTECTION ON THE PROPERTIES OF PEPTIDES CONTAINING PROLINE

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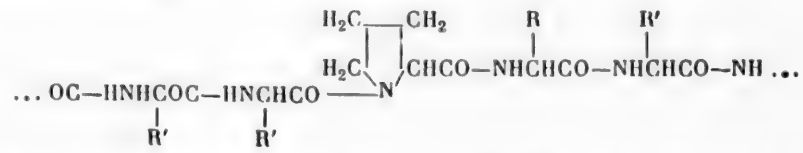
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3931-3938, December, 1960
Original article submitted April 17, 1960

This work is a continuation of our study of the mutual effects of atoms in peptides containing a tertiary nitrogen atom, either in a terminal position or in a peptide bond.

It was reported in a preceding communication [1] that through spectrophotometric measurements made on copper complexes it is possible to observe the change in the character of light absorption in media of different alkalinity as a function of the structure of peptides containing a tertiary nitrogen atom and those in which the amino group is protected.

Particular attention was given to proline in the present work, since the presence of this amino acid in a polypeptide chain naturally changes the character of its light absorption owing to the lack of an enolizable hydrogen on the nitrogen atom. As a consequence, when proline participates in the formation of a peptide chain, there are certain regularities in the absorption spectra which depend on the number of peptide bonds. Thus, for example, the presence of proline and sarcosine as the second amino acid in di- and tripeptides renders this compound incapable of undergoing a biuret reaction [2]. When two or three amino acid residues are present in the peptide chain before the proline residue, the peptide is capable of forming biuret complexes in which the proline residue does not participate [3]. The inclusion of proline or any other amino acid with a tertiary nitrogen atom in a more complex peptide chain in effect disrupts the continuity of the chain, dividing it into shorter sections. Like cyclic or aliphatic groups, the hexamethylenebiscarbamino radical [4] for example, proline interrupts the peptide chain, and each section of the chain before and after the proline forms a complex independently. This can be schematically represented as follows:



Now if in this connection one considers the order of alternation of the amino acids in the collagen molecule (albumin, the richest in proline), then it is possible to state with assurance that proline here disrupts the continuity of the polypeptide chain, and the character of the light absorption associated with the biuret reaction will depend on the presence of the proline and the steric configuration of the polypeptide chain [5].

It should be noted, as a matter of fact, that proline has a great tendency to take part in the formation of rings [6-9], since, as a consequence of its own cyclic nature, it is capable of changing the configuration of a

TABLE 1

Value of λ_{max} (mμ) at Different Concentrations of the Base

Compound	λ_{max} mμ				Δλ
	concentration of base (grams per 10 ml)				
	0.05	0.08	0.24	0.5	
Prolylglycylglycine hydrochloride	560 mμ	—	—	570	10
Ethyl ester of N-carbobenzoxyprolylglycylglycine	—	—	—	590	—
Ethyl ester of N-benzylprolylglycylglycine	—	510	570	—	60

TABLE 2

Values of λ_{max} for the Ester and the Free Tripeptide

Compound	λ_{max} mμ	
	concentration of base (grams per 10 ml)	
	0.05	0.5
Ethyl ester of DL-prolylglycylglycine	560	570
DL-Prolylglycylglycine	560	570

polypeptide chain [10]. For this reason, it seemed of interest to determine its significance in the formation of copper biuret complexes of tetrapeptides and, in the future, higher polypeptides. It was especially interesting to observe the new regularities which hold when the peptide chain contains a terminal tertiary nitrogen atom in addition to a proline residue. This made it possible to determine the role of proline in a peptide of similar configuration. Moreover, we were also interested in the question of the effect of an alkyl or acyl group with the proline at the extremity of the peptide structure.

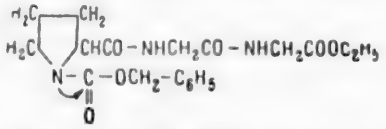
DISCUSSION

The copper complexes studied in the present work were some which we had synthesized previously [11]. The investigation of copper complexes of the ethyl ester of N-benzylprolylglycylglycine (II) and N-carbobenzoxyprolylglycylglycine (I) showed that (I) does not form a copper complex when the concentration of base is low. Only at a concentration of 1.25 N was there formed a complex of the dipeptide type with a λ_{max} 590 mμ; the intensity was very low at the usual peptide concentration (0.01 M).

Substance (II) formed two copper complexes at alkali concentrations of 0.02 and 0.6 N and in the presence of the same amount of copper and the same concentration of the compound, 0.01 N; the complexes had values of λ_{max} of 510 mμ and 570 mμ.

DL-Prolylglycylglycine hydrochloride at base concentrations of 0.04 and 0.4 N and with equal amounts of copper and equal concentrations of the hydrochloride gave complexes for which the shift in the absorption maximum was very slight: λ_{max} 560 and 570 mμ (Table 1).

The difference in the nature of complex formation due to the effect of protective groups is apparent from these data: the carbobenzoxy radical is an acyl protective group, and the benzyl radical is an alkyl protective group. The addition of a carbobenzoxy group to the secondary nitrogen atom of the proline converts it to a tertiary nitrogen, and, in all probability, it is incapable of taking part in complex formation.



If the tertiary nitrogen atom of dibenzyl peptides differs from the nitrogen of an amino group in being more positive, then when the protective group is carbobenzoxy, there will not be an increase in the electron density at the nitrogen atom, but instead there will be repulsion of electrons away from the nitrogen and a suppression of its positive properties. This property of the nitrogen atom of carbobenzoxyproline is confirmed by the inability of this compound to form a hydrochloride.

After removal of the carbobenzoxy group, prolylglycylglycine forms a copper complex with a typical tripeptide absorption spectrum (Table 1).

The ethyl ester of prolylglycylglycine gave the same values of the absorption maximums as were obtained for the peptide itself. Consequently, the ester group has no effect on the position of λ_{max}. It is probable that as the ester stands in an alkaline medium, the ester group is saponified to a carboxyl (Table 2).

The stability of the copper complex of prolylglycylglycine was low at higher concentrations of the base. Over a period of several days the absorption maximum shifted toward the longer wavelengths (λ_{max} 595 mμ) and approached the absorption maximum for a dipeptide copper complex. This shift can possibly be explained by hydrolysis of the peptide at the prolyl–glycine bond–a process which takes place more rapidly at higher concentrations of the base.

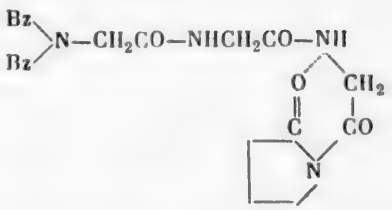
Double complex formation was evident in the case of N-benzylprolylglycylglycine and this may be explained by the influence of alkyl protection at the proline nitrogen atom (Table 1).

Thus, it may be concluded that the first condition which must be satisfied for double complex formation is the presence of a terminal nitrogen atom; however, this condition is not sufficient. The second condition is that the tertiary nitrogen atom must be bonded by one of its own valences with an alkyl group.

Two copper complexes are formed when a tetrapeptide molecule contains two tertiary nitrogen atoms, one of which is a terminal nitrogen with dibenzyl protection and the other is present in the proline residue. Thus, the methyl ester of N,N-dibenzyldiglycylglycylproline forms complexes with λ_{max} of 510 and 580 mμ at base concentrations of 0.02 and 0.3 N with the same amount of copper in each case. In addition, we followed the kinetics of the formation of the copper complex of this compound at a base concentration of 0.01 N. The measurements were carried out every 15 min over a period of an hour. It was found that during the reaction there is a shift in the absorption maximum toward the shorter wavelengths from λ_{max} 550 to λ_{max} 510 mμ. This is accompanied by an increase in the intensity of absorption. Spectrophotometric measurements of this same compound over a period of two days revealed no further change in the position of the absorption maximum (λ_{max} 510 mμ), but the intensity increased significantly.

We shall not attempt to formulate any final conclusions on the basis of these preliminary data, but we do propose that a proline residue in a peptide molecule changes the conformation of the chain. It is known from the literature that proline peptides have a considerable tendency toward coiling of the peptide chain and the formation of intramolecular hydrogen bonds [12, 13]. Our results suggest that in proline-containing peptides there is a change in the geometry of the molecule and possibly the formation of hydrogen bonds, which are broken in an alkaline medium and change the character of light absorption.

This may be represented schematically as follows:



Obviously, such an assumption requires confirmation by x-ray structural investigations.

A comparison of the absorption spectra of the dibenzyltetrapeptide and the dibenzyltripeptide for the same base concentrations showed that these compounds behave differently. Thus, it was only in the case of the tetrapeptide that we were able to observe first the formation of a blue complex and then a shift toward the shorter wavelengths and an increase in absorption intensity. Obviously, this is associated with the presence in the tetrapeptide of two tertiary nitrogen atoms.

After removal of the dibenzyl protection, the methyl ester of triglycylproline gave a single copper complex at concentrations of base from 0.04 to 0.4 N; the maximum was at 550 mμ. It may be possible to explain the position of the maximum on the basis of an effect of the proline, since in ordinary tetrapeptides λ_{max} 525 mμ (triglycylglycine) and for tripeptides λ_{max} 570 mμ. We are not yet in a position to establish the nature of this effect. It is possible that the tertiary nitrogen of the proline takes part to some extent in the formation of the complex; however, this requires confirmation by a large amount of experimental data. In the present work, we have made a first attempt to study the effect of a proline ring in polypeptides on the nature of complex formation.

EXPERIMENTAL

The copper complexes of the peptides and their derivatives were prepared with the following amounts of reagents: into 10 ml of solvent (water, 96% alcohol, or a 1 : 1 mixture of alcohol and water) was introduced that amount of the compound calculated to yield a concentration of 0.01 M, the specified amount of NaOH, and 0.2-0.5 ml of an 0.25 M solution of copper sulfate.

Figures showing the absorption spectra of the copper complexes are presented below (Figs. 1-8).

The copper complex of the ethyl ester of N-carbobenzoxy-DL-prolylglycylglycine had a λ_{max} of 590 mμ (Fig. 1).

The copper complex of the ethyl ester of DL-prolylglycylglycine had λ_{max} of 560 and 570 mμ (Fig. 2).

The copper complex of DL-prolylglycylglycine had λ_{max} of 560 and 570 mμ (Fig. 3).

The copper complex of the ethyl ester of N-benzyl-DL-prolylglycylglycine had λ_{max} of 510 and 570 mμ (Fig. 4).

The copper complex of N,N-dibenzyldiglycylglycine had λ_{max} 550 and of 580 mμ (Fig. 5).

The copper complex of the methyl ester of N,N-dibenzyltriglycyl-DL-proline had λ_{max} of 520 and 580 mμ (Fig. 6).

The copper complex of the methyl ester of triglycylproline had a λ_{max} of 550 mμ (Fig. 6, curve 3).

Complexes with the same amount of peptide and the same amount of copper were prepared in the presence of 0.004 g of NaOH at the same time.

The kinetics of the formation of the complex as determined by measurements at various time intervals are presented in Table 3 (Fig. 7).

The copper complex of N,N-diethylnorleucylglycylglycine had λ_{max} of 520 and 590 mμ (Fig. 8).

The copper complex of norleucylglycylglycine had a λ_{max} of 570 mμ (Fig. 8).

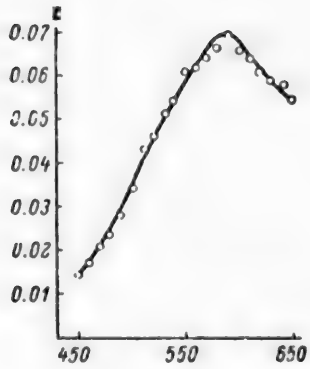


Fig. 1. Absorption spectra of the copper complex of the ethyl ester of N-carbobenzoxy-DL-prolylglycylglycine. Medium: water–alcohol, 1 : 1.

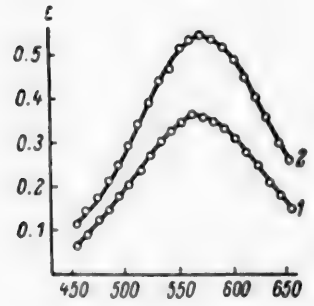


Fig. 2. Absorption spectra of the copper complex of the ethyl ester of DL-prolylglycylglycine. Medium: water; weight of NaOH (in g): 1) 0.05, 2) 0.5.

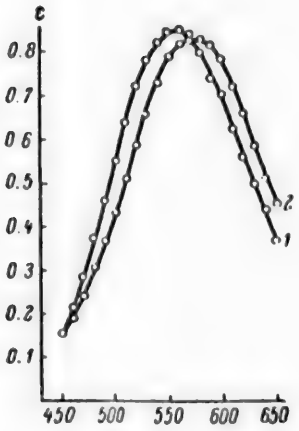


Fig. 3. Absorption spectra of the copper complex of DL-prolylglycylglycine. Medium: water; notation for curves is the same as in Fig. 2.

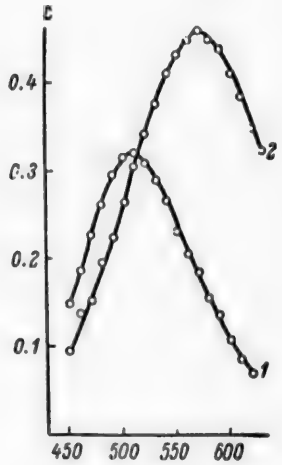


Fig. 4. Absorption spectra of the copper complex of the ethyl ester of N-benzyl-DL-prolylglycylglycine. Medium: alcohol–water; weight of NaOH (in g): 1) 0.008, 2) 0.24.

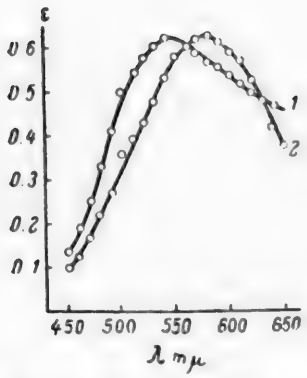


Fig. 5. Absorption spectra of the copper complex of N,N-dibenzyldiglycylglycine. Medium: 96% alcohol; weight of NaOH (in g): 1) 0.008, 2) 0.12.

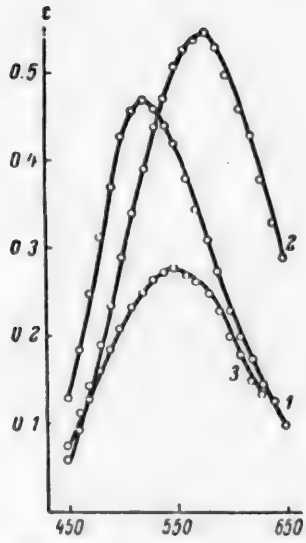


Fig. 6. Absorption spectra of the copper complex of the methyl ester of N,N-dibenzyltriglycyl-DL-proline (1 and 2) and of the methyl ester of triglycylproline (3, medium: 96% alcohol). Medium: alcohol–water; weight of NaOH (in g): 1) 0.008, 2) 0.12, 3) 0.16.

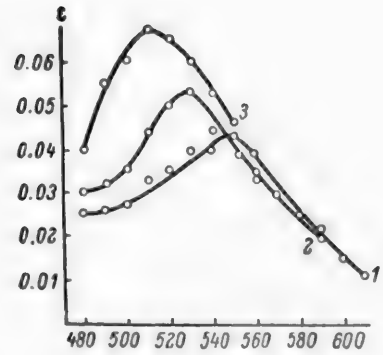


Fig. 7. Change in the absorption spectrum of the copper complex of the methyl ester of N,N-dibenzyltriglycylproline with time. Medium: water–alcohol; weight of NaOH, 0.004 g; 1) λ_{max} 550 mμ at 15 min after formation, ε = 0.074; 2) λ_{max} 530 mμ at 30 min, ε 0.083; 3) λ_{max} 510 mμ after 2 days, ε 0.1550.

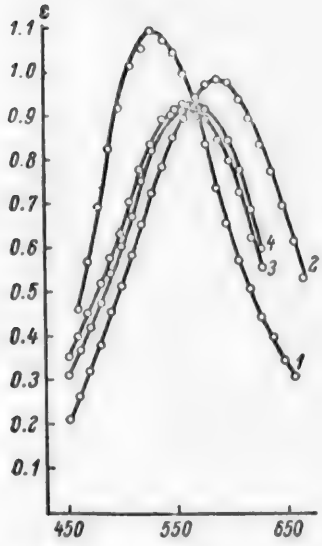


Fig. 8. Absorption spectra of N,N-diethylnorleucyl- (1 and 2) and norleucylglycylglycine (3 and 4). Medium: water (1, 2); weight of NaOH (in g): 1) 0.008, 2) 0.24, 3) 0.05, 4) 0.4.

TABLE 3

The Change in the Absorption Spectra of Copper Complexes of a Tetrapeptide with Time (weight of base, 0.004 g; solvent, alcohol + water)

λ, mμ	Methyl ester of N,N-dibenzyldiglycylglycylproline					
	15 min after formation	after 30 min	after 45 min	after 60 min	after 75 min	after 2 days
500	0.057	0.065	0.083	0.090	0.090	0.130
510	0.063	0.074	0.085	0.090	**0.097***	**0.155***
520	0.065	0.080	**0.088***	**0.092***	0.095	0.152
530	0.066	**0.083***	0.085	0.089	0.090	0.150
540	0.070	0.074	0.080	0.082	0.083	0.143
550	**0.074***	0.069	0.075	0.075	0.076	0.130
560	0.063	0.063	0.069	0.065	0.066	0.120
570	0.060	0.060	0.060	0.059	0.057	0.115
580	0.055	0.059	0.055	0.051	0.050	0.082
590	0.052	0.050	0.048	0.048	0.049	0.079
600	0.045	0.045	0.045	0.046	0.044	0.076

*Figures in bold-face type denote maximum optical density.

SUMMARY

1. New data were obtained on the formation of two types of complexes by N,N-dialkyl substituted tripeptides with copper ions at different concentrations of base.

2. The ability of a proline tripeptide protected by an acyl group to form complexes has been compared with that of alkyl-protected tripeptides.

It was shown that the ethyl ester of N-carbobenzoxyprolylglycylglycine does not form a copper complex at low base concentrations. With an increase in the concentration of the base (1.25 N) λ_{max} becomes 590 mμ, but the intensity of the spectrum is very low (ϵ_{max} 0.0711).

The ethyl ester of N-benzylprolylglycylglycine forms two copper complexes at base concentrations of 0.02 and 0.6 N: λ_{max} of 510 and 570 mμ. Prolylglycylglycine has λ_{max} of 560 and 570 mμ under these same conditions.

3. The nature of the formation of copper complexes of N,N-dibenzyl-substituted and of free proline-containing peptides was studied.

It was shown that the ethyl ester of N,N-dibenzyltriglycylproline forms first a blue complex (λ_{max} of 520 mμ) and then red complex (λ_{max} of 580 mμ) with a simultaneous increase in the intensity of absorption; this is associated with the presence in the tetrapeptide of two tertiary nitrogen atoms.

The unprotected methyl ester of triglycylproline had a λ_{max} of 550 mμ regardless of the concentration of the base.

4. A difference was noted in the formation of copper complexes by the tetrapeptide as compared to other peptides lacking a tertiary nitrogen atom.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**

ON THE STEREOSPECIFICITY OF THE INTERACTION OF ESTERS OF STEREOISOMERIC 1,4-CYCLOHEXANEDICARBOXYLIC ACIDS WITH GRIGNARD REAGENTS

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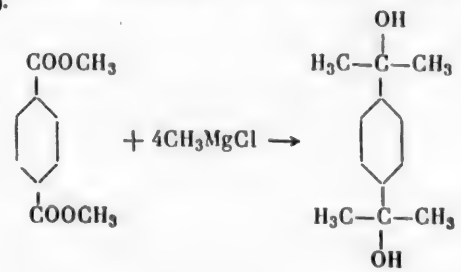
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3938-3945, December, 1960
Original article submitted February 1, 1960

In connection with the great interest which has, in recent years, been responsible for stereochemical investigations in the field of cis–trans-isomerism of alicyclic compounds, it is very important to determine which of those reactions ordinarily used for the conversion of compounds into others take place stereospecifically. In particular, it is desirable to know what routes can be used to carry out given conversions in the side chains of disubstituted cyclanes without disturbing the steric disposition of these chains. It has been considered that if the reaction does not involve the bond between the ring atom to which the side chain is attached and the first atom of the chain, there should be no change in the configuration of the stereoisomer; however, in the case of many reactions in which the bond is not involved at all, the reaction products nevertheless include a certain amount of the other stereoisomer, which is frequently difficult to separate. Thus, for example, when lithium aluminum hydride reacts with one of the tosylates of the individual stereoisomeric 1,3-dimethylcyclopentanes, the resulting cis- or trans-1,3-dialkylcyclopentane will include up to 17% of the corresponding stereoisomer [1], even though the bonds between the ring carbon atoms and the methylol groups do not take part in this reaction. At the same time, certain other reactions take place strictly stereospecifically, for example, the reduction of carbalkoxy and carboxyl groups by this same lithium aluminum hydride [2,3].

Since the stereochemistry of some of the alicyclic dicarboxylic acids has been well studied and their individual stereoisomers are frequently comparatively available, they should be useful as starting materials for the preparation of numerous stereoisomeric substances. On the basis of these considerations, we decided to determine whether the reaction of such esters with Grignard reagents takes place stereospecifically.

The compounds selected for this investigation were the cis- and trans-1,4-cyclohexanedicarboxylic acids, the configurations of which have repeatedly been established by various methods [4, 5], so that this feature of the investigation could not raise any doubts. The dimethyl ester of the cis-acid has been prepared by the action of diazomethane on the acid [4], so that the configurations of the esters of these acids must also be considered reliably established. Therefore, the dimethyl esters of the cis- and trans-acids were reacted with the Grignard reagent (methylmagnesium halide).



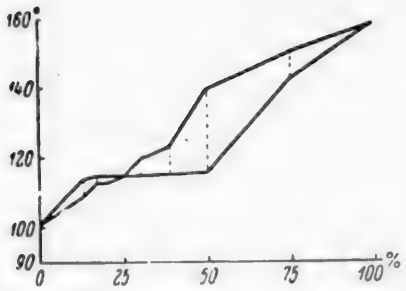


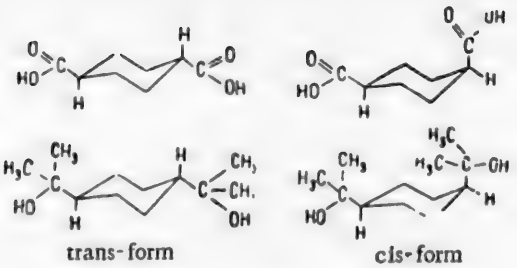
Fig 1. Dependence of the melting point of mixtures of cis- and trans-1,4-bis(α-hydroxyisopropyl)cyclohexanes on composition of the mixture. The lower broken line joins points corresponding to the beginning of melting; the upper line represents the end of melting.

However, it was found that apparently the reaction proceeds stereospecifically only in the case of the trans-isomer. At least, it was only from the ester of the trans-acid that there was obtained a single 1,4-bis(α-hydroxyisopropyl)cyclohexane, which had an m.p. of 159.3-159.8°. From the interaction of the Grignard reagent with the ester of the cis-acid we invariably obtained a mixture which melted over a wide temperature range. Two substances with sharp melting points, 100.9-101.2° and 115.5-116.0°, were obtained by fractional crystallization of this mixture. The analysis of each substance corresponded to the composition $C_{12}H_{24}O_2$, as did that of the trans-diol. It was found that the second substance could easily be obtained from the first substance and the trans-diol. This could be accomplished simply by mixing them in a weight ratio of 3 : 1, respectively, dissolving the mixture in chloroform at room temperature, and evaporating the solvent, also without heating. The preparation obtained by this route melted sharply at 115.5-116.0°, and a mixture of this material with the second substance obtained from the products of the Grignard reaction melted without depression of the melting point. As may be seen from Fig. 1, no other ratio of the first substance to the trans-diol gave a preparation with a sharp melting point. This led us to the conclusion that the first substance, which melted at 100.9-101.2°, was cis-1,4-bis(α-hydroxyisopropyl)cyclohexane; correspondingly, the substance with an m.p. of 159.3-159.8° was the trans-isomer. This conclusion is consistent with the fact that the trans-isomer was obtained as the sole product from the interaction of the ester of the trans-acid with the Grignard reagent and also with the fact that a higher melting point is characteristic of the trans-form in the series of 1,4-disubstituted cyclohexanes. In particular, between the two 1,4-dimethylcyclohexanes, which are structurally close to our compounds, the trans-compound also has the higher melting point [3].

The second substance, m.p. 115.5-116.0°, was apparently a molecular compound of three molecules of the cis-diol and one molecule of the trans-diol. Consequently, the reaction of the ester of the cis-acid with the organomagnesium compound was not stereospecific, and the small amount of trans-diol formed combined with cis-diol during the course of the reaction. The fraction of the molecular compound among the reaction products varied in different syntheses over the range of 45 to 100%, and we were unable to establish on which of the insignificant changes in reaction conditions this depended. The molecular compound formed by the individual stereoisomers was extremely stable. We made numerous attempts to separate it into the individual stereoisomers by fractional crystallization from various solvents (water, methanol, ethanol, ether, acetone, n-hexane, dioxane, and chloroform), by chromatography on silica gel or aluminum oxide, and by paper chromatography (from various solvents in both types of chromatography), but all attempts were unsuccessful. We were successful only in separating a small amount of crystals of the trans-diol from the molecular compound; these crystals melted at about 159°, and a mixture with known trans-diol melted without depression of the melting point.

It is also possible that the ability of cis- and trans-isomers to form molecular compounds is also inherent in other substances of similar structure. Thus, there is an indication in the literature [4] that a substance with an m.p. of 166-167°, which has been described as cis-1,4-cyclohexanedicarboxylic acid, is actually a mixture of the cis- and trans-forms (6% trans-acid), even though it melted within a narrow temperature interval. Neither the composition nor the melting point of this mixture changed upon repeated crystallizations. According to the literature [4], the pure cis-acid (m.p. 170-171°) can be prepared only by hydrolysis of the cyclic anhydride of this acid. A synthetic mixture of the pure cis-acid with the trans-acid melted at 166-167°, and it, too, could not be separated by crystallization.

We shall now turn our attention to the great similarity between our compounds and those obtained by the Polish authors [4]. In addition to the fact that they are all 1,4-disubstituted cyclohexanes, they are also all symmetrically substituted with oxygen atoms in the 1- and 1'-positions in the side chains. This similarity is clearly apparent from the structural formulas:



trans-form cis-form

One is inclined to suspect that in both cases the molecular compounds are formed by hydrogen bonding, or else they are inclusion compounds. One piece of evidence against the first proposal is that the Polish authors [4] prepared a dimethyl ester with an m.p. of 14° from their cis-acid, while our purest preparation of this substance, which was prepared by a different route, froze at 9.6°, although, as far as may be judged from the freezing point curve, it had a purity of 99.8%. Therefore, the possibility cannot be excluded that we were dealing in this case with a molecular compound and that the high degree of purity related to the latter compound and not to an individual dimethyl ester of the cis-acid. Moreover, esters of 1,4-cyclohexanedicarboxylic acids, despite the fact that they have oxygen atoms at the 1- and 1'-positions in the side chains, do not have labile hydrogen atoms, and cannot, therefore, form hydrogen bonds. On the other hand, our preparation of the ester of the cis-acid cannot be an inclusion compound, since such a compound by its very nature can exist only in the solid form. Considering all of these indications, we believe that only further study of the properties of the dimethyl ester of cis-1,4-cyclohexanedicarboxylic acid can shed light on this problem.

We remark, by the way, that our conclusion as to the nonstereospecific course of the Grignard reaction with the ester of the cis-acid is correct regardless of whether the preparation we used in the reaction was an individual compound or a molecular compound of the cis- and trans-forms. It is evident that in the latter case the yield of molecular compound of the diols from a stereospecific reaction should have been constant in all experiments, since the concentration of ester of the trans-acid in the starting material was constant, and this was not observed.

Since we had available pure cis- and trans-diols, we naturally attempted to prepare some new stereoisomeric derivatives of 1,4-diisopropylcyclohexane. We first attempted to prepare cis- and trans-1,4-bis(α-chloroisopropyl)cyclohexanes and their bromine and iodine analogs; however, we were able to accomplish the synthesis of these compounds only in the case of the trans-compounds, since replacement of the hydroxyl in the cis-diol by chlorine was accompanied by partial isomerization to the trans-form, even at −30°. We were unable to separate the resulting mixture of dichlorides into individual stereoisomers by crystallization.

The trans-form of the dichloride, dibromide, and diiodide was, in each case, a crystalline material which readily decomposed on comparatively slight heating. Thus, the dichloride decomposed during crystallization from boiling methanol and even on prolonged boiling in ether solution. The dibromide could be recrystallized from ether only with difficulty, and only a small part of the diiodide was recovered from a similar recrystallization. On standing at ambient conditions for several weeks, the diiodide was converted to a dark liquid with the odor of hydrogen iodide.

In conclusion, it should be remarked that in contradiction to the rule of Auwers-Skita, the dimethyl ester of cis-1,4-cyclohexanedicarboxylic acid boiled lower than its trans-stereoisomer. Two such violators of the rule have recently been encountered among the 1,4-disubstituted cyclohexanes: the 1,4-diisopropylcyclohexanes [6] and the 4-methylcyclohexanols [7].

EXPERIMENTAL

The dimethyl esters of cis- and trans-1,4-cyclohexanedicarboxylic acids. To a two-liter autoclave was charged 350 g of dimethyl terephthalate, 350 ml of methanol, and 50 ml of Raney nickel. The hydrogenation was carried out at 185-200°* and an initial hydrogen pressure of 140-150 atm. The hydrogenation proceeded very poorly at a lower initial pressure. The catalyst was removed by filtration, the methanol was distilled, and

*At a higher temperature, even at 210°, there was considerable decomposition with a sharp increase in the pressure in the autoclave.

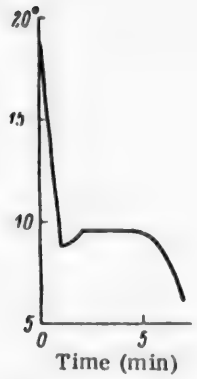


Fig. 2. Freezing-point curve for the dimethyl ester of cis-1,4-cyclohexanedicarboxylic acid.

the residue was distilled under vacuum. The distillation yielded the dimethyl ester of 1,4-cyclohexanedicarboxylic acid – chiefly the cis-form; the yield was 65% of material with a b.p. of 148-151.5° (19 mm). There were also obtained 6% of a substance with a b.p. of 87.0-90.0° (19 mm) (possibly the methyl ester of hexahydrobenzoic acid formed by decarboxylation), 23% of a crystalline mass from which was separated (in small portions) the dimethyl ester of trans-1,4-cyclohexanedicarboxylic acid with an m.p. of 68.5-69.5° (from ether), and a substance with an m.p. of 105.5-106.0° (from ether). This last material was apparently the previously undescribed monomethyl ester of cis-1,4-cyclohexanedicarboxylic acid, since analysis of the material indicated the correct composition, and it melted significantly lower than the monomethyl ester of the trans-acid (m.p. 125° [8]).

Found %: C 58.21, 58.07; H 7.52, 7.62. $C_9H_{14}O_4$. Calculated %: C 58.05; H 7.58.

The same route was used, in several experiments, to prepare 2957 g of the major fraction of the dimethyl ester of 1,4-cyclohexanedicarboxylic acid. Cooling this fraction with an ice-salt mixture caused the entire mass to crystallize, but when the mass was allowed to warm slowly to room temperature, not all of it melted, and a considerable part of the trans-form remained in the form of crystals. The dimethyl ester of the trans-acid was separated by filtration and repeatedly recrystallized; it melted at 70.0-70.5° [9].

It was subsequently found that it was easier to convert this material to trans-1,4-bis(α-hydroxyisopropyl)-cyclohexane and to purify the latter than to purify the ester itself, and, therefore, in succeeding syntheses less pure portions of the ester with a melting point not lower than 68° were used.

The dimethyl ester of the cis-acid was distilled in a glass-packed column with an efficiency of about 60 theoretical plates, and was then purified by repeated recrystallization from ether at low temperatures followed by redistillation in the same column. The purest fraction had a b.p. of 126.9-127.2° (7 mm), f.p. 9.6°, $n^{20}D$ 1.4590, d^{20}_4 1.1111, and was 99.8% pure. The freezing point curve for the ester of the cis-acid is shown in Fig. 2. The cryoscopic constants of the esters were determined by adding the other stereoisomer; they were: 0.030 and 0.035 mole fraction/degree of the cis- and trans-forms, respectively.

During the initial distillation of the mixture of stereoisomeric esters, it was observed that the trans-isomer accumulated in the last fractions of distillate and in the residue. Thus, in one of the distillations, crystals of the trans-isomer appeared in fractions collected after distillation of 61% of the mixture charged (762 g), and the distillation residue (21%) completely crystallized.

Trans-1,4-bis(α-hydroxyisopropyl)cyclohexane. Into a four-neck flask fitted with a stirrer with mercury seal, a reflux condenser, a dropping funnel, a thermometer with a long stem reaching to the bottom of the flask, and a gas-inlet tube was placed 24 g of magnesium and 800 ml of absolute ether, and the air was displaced by methyl chloride dried over sulfuric acid and silica gel. The contents of the flask were then cooled to 15°, the stirrer was started, and methyl chloride was rapidly fed into the flask. At this temperature, absorption of the methyl chloride was very rapid. When all of the magnesium had reacted, the stream of methyl chloride was replaced by a stream of nitrogen, and to the flask was rapidly added a solution of 24 g of the dimethyl ester of trans-1,4-cyclohexane dicarboxylic acid (m.p. 70.0-70.5°) in 120 ml of ether. The reaction mixture was then heated on a water bath to the boiling point of the ether, and was stirred at this temperature for 5 hr; it was then allowed to stand overnight. The Grignard complex was decomposed first with water and then with hydrochloric acid. Owing to the very low solubility of the trans-diol in ether, a large part of it appeared as a crystalline suspension in the ether layer. After the crystals had been removed by filtration, the lower layer was separated and discarded, and the ether layer was washed three times wtih bisulfite solution and then with water, a solution of sodium carbonate, and again with water. It was then dried and evaporated to a small volume. This resulted in precipitation of crystals, which were separated by filtration and combined with the material obtained by the first crystallization. The yield of dried crystals was 80-85% in several syntheses. The material was a fine powder with an m.p. of 159.3-159.8° (from acetone).

Found %: C 71.84, 71.89; H 11.85, 11.91. $C_{12}H_{24}O_2$. Calculated %: C 71.95; H 12.08.

Dependence of the Melting Point of Mixtures of cis- and trans-Diols on the Composition of the Mixture

Mixture No.	Content of trans-form (in %)	Melting range
1	0	100.9—101.2°
2	12.8	109.0—114.0
3	17.1	113.0—115.0
4	20.0	113.5—115.0
5	25.0	115.5—116.0
6	25.0	115.0—115.5
7	30.0	115.0—116.5
8	33.3	116—124
9	50.0	116—140
10	75.0	143—151
11	100	159.3—159.8

Trans-1,4-bis(α-chloroisopropyl)cyclohexane. A solution of 10.0 g of trans-1,4-bis(α-hydroxyisopropyl)cyclohexane in 100 ml of methanol was cooled with ice, and dry hydrogen chloride was then passed into the solution until there was no further increase in weight. The dichloride precipitated. The precipitate was separated by filtration, washed twice with cold methanol, and dried in air; the weight of the precipitate was 11.3 g (95.7%). Several recrystallizations from ether yielded 9.4 g (79.7%) of the dichloride in the form of lustrous leaflets.* M.p. 135.6-136.3°.

Found %: C 60.81, 60.93; H 9.34, 9.38; Cl 29.71, 29.73. $C_{12}H_{24}Cl_2$. Calculated %: C 60.71; H 9.35; Cl 29.88.

Trans-1,4-bis(α-bromoisopropyl)cyclohexane. A solution of 2.0 g of trans-1,4-bis(α-hydroxyisopropyl)cyclohexane in 50 ml of methanol was cooled with ice, and dry hydrogen bromide was passed into the solution until there was no further increase in weight. The dibromide precipitated and was treated in the same manner as the dichloride. The weight of the dry dibromide was 2.6 g (79.3%). Several recrystallizations from ether yielded lustrous leaflets with an m.p. of 146.5-147.0° (in a sealed capillary).

Found %: C 44.18, 44.34; H 6.82, 6.73; Br 49.03, 49.03. $C_{12}H_{24}Br_2$. Calculated %: C 44.19; H 6.80; Br 49.01.

Trans-1,4-bis(α-iodoisopropyl)cyclohexane. A solution of 3.0 g of trans-1,4-bis(α-hydroxyisopropyl)cyclohexane in 75 ml of methanol was cooled with ice, and dry hydrogen iodide was passed into the solution until there was no further increase in weight. The reaction products were treated in the same manner as in the preceding cases, and there was obtained 3.1 g (49.2%) of the dry diiodide. Recrystallization of 1.4 g of the diiodide from ether gave 0.7 g of crystals (lustrous leaflets) having a sharp decomposition temperature of 66.2-66.5° (in a sealed capillary).

Found %: C 34.32, 34.04; H 5.29, 5.25; I 60.12, 60.46. $C_{12}H_{24}I_2$. Calculated %: C 34.28; H 5.24; I 60.48.

Cis-1,4-bis(α-hydroxyisopropyl)cyclohexane. Grignard reagents were prepared from 25 g of magnesium in 220 ml of absolute ether and methyl bromide in the same manner used in the synthesis of the trans-diol. Then, at a temperature of 10-12°, was added 25.0 g of the dimethyl ester of cis-1,4-cyclohexanedicarboxylic acid (m.p. 9.6°) in 120 ml of absolute ether. The reaction mixture was stirred for 2 hr at 20-25°, and was then allowed to stand overnight. The complex was decomposed with ice and hydrochloric acid, and the precipitated crystals of cis-diol were separated by filtration and dried; the yield of dry crystals was 21.1 g (84.4%). The ether layer was discarded. Fractional crystallization from ether gave 7.6 g (30%) of a compound with an m.p. of 100.9-101.2° (after drying at 70° for 2 hr); the residue from the fractional crystallization was a compound with an m.p. of 115.5-116.0°.

Substance with an m.p. of 100.9-102°. Found %: C 71.75, 71.74; H 12.04, 11.95.

Substance with an m.p. of 115.5-116°. Found %: C 71.84, 71.88; H 11.95, 12.12. $C_{12}H_{24}O_2$. Calculated %: C 71.95; H 12.08.

Upon crystallization from water or wet ether, the first substance formed a monohydrate which melted when heated rapidly at an indeterminate temperature below 90°. When heated slowly, it readily lost water, and the resulting anhydrous compound melted at about 101°.

Found %: H_2O 9.10, 8.67. $C_{12}H_{24}O_2 \cdot H_2O$. Calculated %: H_2O 8.99.

Synthetic mixtures of cis- and trans-diols. Synthetic mixtures of the anhydrous cis-diol (m.p. 100.9-101.2°) and trans-diol were prepared by dissolving small weighed amounts of the diols in chloroform and evaporating the chloroform. All of these operations were carried out at room temperature. The results of the melting point determinations on these mixtures are shown in Fig. 1 and in the table.

*When the crystals were grown slowly, regular hexahedrons and elongated hexahedral plates are obtained.

A mixture prepared from the synthetic mixture (No. 6 of the table) and the material with an m.p. of 115.5-116.0° obtained in the synthesis described above melted at 115.0-115.7°.

Cis-1,4-bis(α-chloroisopropyl)cyclohexane. a) A solution of 0.9 g of cis-1,4-bis(α-hydroxyisopropyl)cyclohexane (m.p. 100.9-101.2°) in 3 ml of methanol was cooled with ice, and dry hydrogen chloride was passed into the solution until there was no further increase in weight. The resulting precipitate was purified as in the case of the trans-isomer; the yield of dry precipitate was 0.8 g (75%). Two fractions were separated by fractional recrystallization from ether; one fraction melted at 131-134° (0.3 g), and the other melted at 75-99.5°.

b) Dry hydrogen chloride was passed into a solution of 2.0 g of the cis-diol (m.p. 100.9-101.2°) in 12 ml of methanol at −30°. After the usual treatment, the precipitate weighed 2.0 g (84%). It was not possible to separate a fraction with a sharp melting point by fractional crystallization.

SUMMARY

1. It was shown that in the reaction of a Grignard reagent with the dimethyl esters of the stereoisomeric 1,4-cyclohexanedicarboxylic acids, the trans-form reacts stereospecifically, while the cis-form reacts with partial conversion to the other configuration.

2. The cis- and trans-1,4-bis(α-hydroxyisopropyl)cyclohexanes, trans-1,4 bis(α-chloroisopropyl)cyclohexane, and the bromine and iodine analogs, none of which have been previously described in the literature, were prepared.

3. It was shown that the stereoisomeric 1,4 bis(α-hydroxyisopropyl)cyclohexanes combine to form a molecular compound.

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CONDENSATION OF CYCLOPENTADIENE WITH ALIPHATIC DIENES

I. THE INTERACTION OF CYCLOPENTADIENE WITH BUTADIENE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3945-3953, December, 1960
Original article submitted February 14, 1960

Bridged bicyclic compounds prepared by Diels-Alder synthesis from cyclopentadiene or its halogen derivatives have recently attracted widespread attention. These compounds are based on the bicyclo(2,2,1)heptane structure. Many of them have found application as insecticides, plasticizers, monomers for the production of heat-proof plastics, etc. Therefore, the synthesis of compounds of this type and the study of their physical and chemical properties are of definite interest.

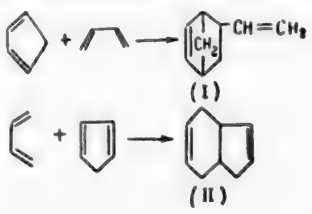
It is well known that dienic hydrocarbons with conjugated double bond systems can undergo Diels-Alder type reactions by themselves; in such reactions, one molecule acts as the diene and another acts as the dienophile. This route yields dicyclopentadiene from cyclopentadiene, vinylcyclohexene from butadiene, etc. This reaction has been quite thoroughly studied. However, the condensation of two different hydrocarbons with conjugated double bonds remains almost without study.

It is known, for example, that piperylene, isoprene, dipropenyl, diisopropenyl, and 1,3-cyclohexadiene are capable of entering into Diels-Alder reactions with butadiene at 150° with the formation of the corresponding codimers [1]. The authors of this paper determined the structure of several of these products, but did not isolate the individual compounds.

It is reported in the literature [2, 3] that cyclopentadiene and methylcyclopentadiene can form codimers with acyclic dienes. This essentially exhausts the presently available information on the cocondensation of different diolefinic hydrocarbons by the Diels-Alder route.

It appeared to us that investigation of this reaction is of definite interest, since in the first place, such an investigation would provide the information necessary for the synthesis of new cyclic hydrocarbons of a given structure, and, in the second place, it would permit a comparison of the relative reactivities of dienic hydrocarbons in the Diels-Alder reaction. Therefore, we undertook an investigation of the cocondensation of cyclopentadiene with butadiene.

It was found that the reaction of cyclopentadiene with butadiene can successfully be applied to the synthesis of both possible codimers—2-vinylbicyclo(2,2,1)-5-heptene (I) and 4,9,7,8-tetrahydroindene (II).

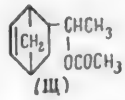


(I)

(II)

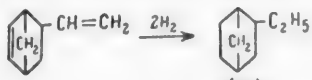
When the reaction is carried out within the temperature range of 140 to 200°, in addition to compounds (I) and (II) there are also formed dimers of butadiene and cyclopentadiene and reaction products of higher molecular weight. By changing the temperature of the experiment, it is possible to direct the condensation toward the predominant formation of either vinylbicycloheptene (I) or tetrahydroindene (II), the first of these compounds being formed at the lower temperatures and the second at the higher temperatures. Thus, when cyclopentadiene and butadiene were heated at 140-145° for 3.5 hr, 18.3% vinylbicycloheptene and 6.2% tetrahydroindene were formed. The yield of tetrahydroindene increased and that of the vinylbicycloheptene decreased with an increase in the reaction temperature. When the reaction was carried out at 170° for 5 hr, 6% vinylbicycloheptene and 17% tetrahydroindene were formed, while 22% tetrahydroindene and traces of vinylbicycloheptene were formed in 2 hr at 210°. The increase in the yield of tetrahydroindene with an increase in reaction temperature was undoubtedly associated with the property of vinylbicycloheptene of isomerizing to tetrahydroindene at elevated temperatures [4].

A. A. Petrov [5] previously attempted to prepare 2-vinylbicyclo-(2,2,1)-5-heptene by pyrolysis of acetate (III); however, they isolated only decomposition products of the latter – cyclopentadiene and butenol acetates.



(III)

2-Vinylbicyclo(2,2,1)-5-heptene reacts with phenyl azide [triazobenzene]. When hydrogenated, it adds two molecules of hydrogen and forms the known 2-ethylbicyclo(2,2,1)heptane (IV) [6].

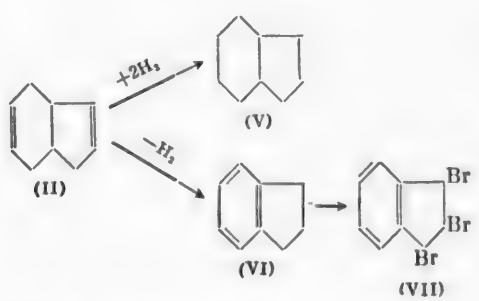


(IV)

We were unable to hydrogenate vinylbicycloheptene selectively at one double bond.

The characteristic structural elements of the molecule – the bicycloheptene system and the vinyl group – were readily apparent in the Raman spectrum of 2-vinylbicyclo (2,2,1)-5-heptene.* The bicycloheptene structure was characterized by a line at 1569 cm^{-1}, which is associated with vibration of the double bond; in addition, other lines characteristic of this structural element were present [7]. The presence of the vinyl group was characterized by lines with frequencies of 1420, 1638, 3001, and 3081 cm^{-1} [7, 8].

The structure of the tetrahydroindene was proved by hydrogenation; it added two molecules of hydrogen with the formation of hydrindane (V). Chromatography of the hydrindane on silica gel and distillation showed that it was the cis-isomer with a trace, about 3%, of the trans-isomer. Fractional distillation gave cis-hydrindane of 99.88% purity. Catalytic dehydrogenation of the tetrahydroindene gave indane (VI); a crystalline derivative of the latter – 1,2,3-tribromoindane (VII) – was prepared.



(II) (V) (VI) (VII)

Vacuum distillation of 107 g of the tetrahydroindene in a column with an efficiency of 100 theoretical plates gave 85.5 g of tetrahydroindene with a b.p. of 72.2° (40 mm). Fifteen fractions were collected during the

*We express our sincere appreciation to V. T. Aleksanyan and Kh. E. Sterin for their study of the Raman spectra, which was carried out at the Commission on Spectroscopy of the Academy of Sciences of the USSR.

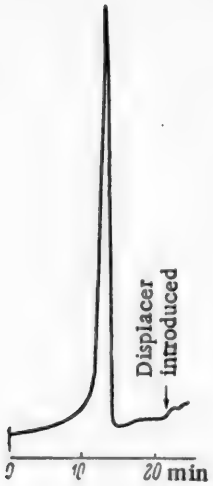


Fig. 1. Chromatogram of tetrahydroindene.

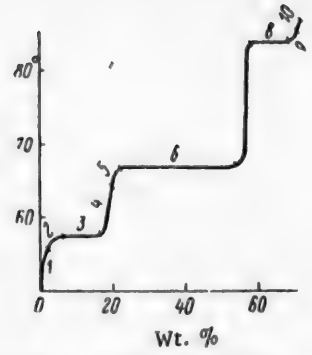
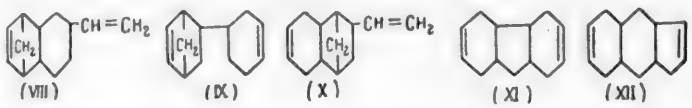


Fig. 2. Distillation of the products of the condensation of cyclopentadiene with butadiene (at 66 mm).

distillation, and the refractive indices and densities of these fractions were all the same ($n^{20}D$ 1.4979, d^{20}_4 0 9261). That the tetrahydroindene was an individual compound and did not contain impurities was shown by gas-liquid chromatography* (the stationary phase was silicone oil of fire brick, the temperature was 150°, the nitrogen rate was 50 ml/min) (Fig. 1). However, during an investigation of the Raman spectrum of the tetrahydroindene it was found that in the region of double bond valence vibrations there were not two lines, as would be expected, but four lines: 1602 (4), 1618 (4), 1637 (4), and 1661 (3) cm^{-1}; all were of approximately equal intensity. There were also four lines in the 1600-1660 cm^{-1} region of the infrared spectrum: 1602 (4.8), 1617.5 (6.6), 1636.5 (8.2), and 1655 (7.8) cm^{-1} [4]. We are still unable to give an explanation of the phenomenon.

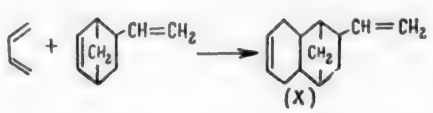
As was mentioned above, in addition to codimers, the condensation of cyclopentadiene with butadiene also yielded products of higher molecular weight. By means of fractional distillation under vacuum, we were able to separate four hydrocarbons from the complex mixture—one of the composition $C_{13}H_{18}$, two of the composition $C_{14}H_{18}$, and one of the composition $C_{15}H_{18}$. The physical properties of these compounds are presented in the table.

If it is assumed that the hydrocarbon with the composition $C_{13}H_{18}$ was formed by Diels-Alder reaction of two molecules of butadiene and one molecule of cyclopentadiene, it could have one of the structures represented by (VIII-XII).



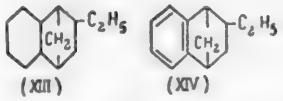
Selection among these structures was made on the basis that the hydrocarbon did not react with phenyl azide, which is a characteristic of compounds having a bicycloheptene double bond [thereby eliminating structures (VIII) and (IX)], and that catalytic dehydrogenation of the carbon yielded only 1 mole of hydrogen [eliminating structures (XI) and (XII)].

That the structure of the hydrocarbon corresponded to 2-vinyl-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene (X) was confirmed by an alternate synthesis by condensation of vinylcycloheptene with butadiene.



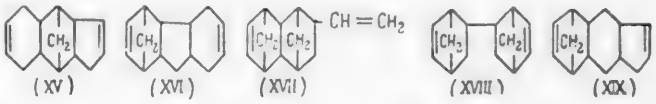
*We are indebted to B. A. Rudenko of the Institute of General Chemistry, Academy of Sciences of the USSR, for carrying out these analyses.

Consequently, the product of the complete hydrogenation of (X) has the structure (XIII), and the dehydrogenation product has the structure (XIV).



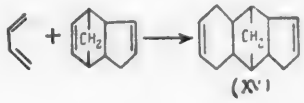
(XIII) (XIV)

The structure of the two hydrocarbons having the composition $C_{14}H_{18}$ was proved in a similar manner. Assuming that each of these was formed from two molecules of cyclopentadiene and one molecule of butadiene, these hydrocarbons could have one of the structures represented by (XV-XIX).



(XV) (XVI) (XVII) (XVIII) (XIX)

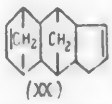
Since neither of the hydrocarbons having the composition $C_{14}H_{18}$ reacted with phenyl azide, structures (XVI-XIX) may be eliminated from further consideration. That one of these hydrocarbons (m.p. 36°) did in fact have the structure corresponding to 2,3-(Δ^1-cyclopenteno-3,4)-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene (XV) was confirmed by the fact that we were able to prepare it by condensation of cyclopentadiene dimer with butadiene.



(XV)

However, we were unable to separate the second hydrocarbon having the composition $C_{14}H_{18}$ from the products of the alternate synthesis. Nevertheless, it is most probable that this hydrocarbon also has the structure (XV) and is a stereoisomer of the hydrocarbon melting at 36°.

The hydrocarbon having the composition $C_{15}H_{18}$ was shown to be a trimer of cyclopentadiene (XX).



(XX)

Thus, it is apparent that all of these high-molecular-weight hydrocarbons, (X), (XV), and (XX), were formed by the further interaction of the bicycloheptene double bond in vinylbicycloheptene or in dicyclopentadiene with butadiene or cyclopentadiene. This once more confirms the activity of this bond when such a compound is used as a dienophile. This distinguishes the bicycloheptene double bond from, for example, the double bond in a six-membered ring, in which, in the case of Diels-Alder condensation of butadiene with vinylcyclohexene, the more reactive vinyl double bond reacts [9].

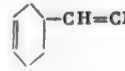
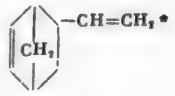
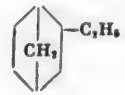
EXPERIMENTAL

Synthesis of 2-vinylbicyclo(2,2,1)heptene and tetrahydroindene. A mixture of 81 g of freshly distilled cyclopentadiene and 70 g of butadiene was heated for 3 hr in a rotating autoclave at 140-145°. The reaction product (138.1 g) was distilled from a Favorskii flask, and a fraction boiling at 40-90° (66 mm) was collected. This fraction contained butadiene dimer, vinylbicycloheptene, and tetrahydroindene (67.8 g). The residue was composed of cyclopentadiene dimer and higher-boiling products. The combined distillate from five experiments was redistilled in a column having an efficiency of 40 theoretical plates.

The results of the fractionation are shown in Fig. 2. The second and third fractions were butadiene dimer, 1-vinyl-3-cyclohexene; the fifth and sixth fractions were 2-vinylbicyclo(2,2,1)-5-heptene (18.3% yield); the eighth and ninth fractions were tetrahydroindene (6.2% yield). The compositions of these hydrocarbons are shown in the table.

The experiments at 170° and 210° were carried out in a similar manner, with the exception that dicyclopentadiene was substituted for cyclopentadiene in the experiment at 210°. Dicyclopentadiene polymerizes under these conditions.

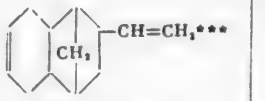
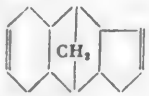
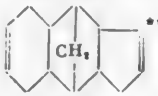
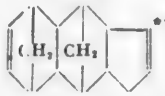
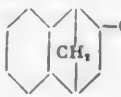
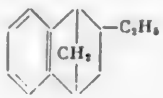
Composition of Hydrocarbons Obtained by Condensation of Cyclopentadiene with Butadiene and Their Hydrogenation and Dehydrogenation Products

№	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Melting point	MR_D found	MR_D calc.	Empirical formula	Yield (in g)	Found (%) C	Found (%) H	Calc. (%) C	Calc. (%) H	Literature source
1		57.7—57.9° (66)	1.4648	—	—	—	—	C_8H_{12}	—	—	—	—	—	[10]
2		67.0 (66), 140.4 (760)	1.4808	0.8884	—	38.48	38.43	C_9H_{12}	—	90.05, 89.92	10.13, 10.16	89.86	10.04	—
3	 cis	84.0—84.2 (66), 160.3 (760)	1.4979	0.9261	—	38.03	38.43	C_9H_{12}	—	89.98, 89.92	10.13, 10.15	89.86	10.04	[11]
4		150—151 (750)	1.4564	0.8562	—	—	—	C_9H_{16}	—	—	—	—	—	[5]
5	 cis	72.5 (33)	1.4720	0.8843	—37.13° ± 0.05	—	—	C_9H_{16}	—	—	—	—	—	[12]
6		73—74 (24)	1.5388	0.9613	—	—	—	C_9H_{10}	—	—	—	—	—	[13]

•Bromine number: found, 243.3, 243.7; calculated, 266.1.

••Bromine number: found, 255.5; calculated, 266.1.

(Continued)

No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Melting point	MR_D found	MR_D calc.	Empirical formula	Yield (in %)	Found (%) C	Found (%) H	Calc. (%) C	Calc. (%) H	Literature source
7		75.0—75.1 (1.5)	1.5145	0.9639	—	54.46	54.70	$C_{13}H_{18}$	13.4	89.53, 89.35	10.32, 10.40	89.58	10.39	—
8		92.5—93.0 (1.5)	—	—	36	—	—	$C_{14}H_{18}$	49.8	90.14, 90.06	9.65, 9.72	90.28	9.72	—
9	 ****	92.5—93(1.5)	1.5391	1.0370	12.5	56.27	57.12	$C_{14}H_{18}$		90.05, 89.90	9.78, 9.93	90.28	9.72	—
10	 *****	103 (2.5)	—	—	66	—	—	$C_{15}H_{18}$	7.4	—	—	—	—	[16]
11		87—89 (44)	1.4920	0.9344	—	55.38	55.63	$C_{13}H_{22}$	—	87.37, 87.26	12.39, 12.44	87.59	12.41	—
12		73—74 (2)	1.5336	0.9683	—	55.26	54.23	$C_{13}H_{16}$	—	90.94, 90.70	9.24, 9.08	90.63	9.36	—

***Mol. wt.: found, 177.1, 174.2; calculated, 174.2.

****Mol. wt.: found, 188.1, 184.8; calculated, 186.2.

*****The adduct with phenyl azide (m.p. 196-197°, from ethyl acetate) was converted by treatment with acetic acid to the corresponding ethylenimine [15] (m.p. 169.5-170.5). Found %: N, 4.99, 4.89. Calculated for $C_{21}H_{23}N$, %: N, 4.84. For literature values for (XXII) see reference [16].

Hydrogenation of the vinylbicycloheptene and tetrahydroindene was carried out in a bomb at ordinary temperatures in the presence of platinum black. Dehydrogenation of the tetrahydroindene was carried out at 300-310° in the presence of platinized carbon (15% Pt). The compositions of the hydrogenation and dehydrogenation products are presented in the table.

Tribromoindane (VII) was prepared from indane by the method of Meyer, and had an m.p. of 134° (from alcohol). The literature [13] reports an m.p. of 134° for (VII). A mixed sample showed no depression of the melting point.

Found %: Br 67.70, 67.50. $C_9H_7Br_3$. Calculated %: Br 67.60.

The interaction of 1 g of vinylbicycloheptene and 2 g of phenyl azide over a period of 22 days gave a thick, viscous mass, but no crystallization was detected. The excess phenyl azide was distilled to separate the addition product, and the residue was analyzed.

Found %: C 74.82, 74.55; H 7.26, 7.23; N 17.77, 17.82. $C_{15}H_{17}N_3$. Calculated %: C 75.27; H 7.16; N 17.56.

The resulting oil was allowed to stand for two years, but it did not crystallize. We may also remark that it was not possible to prepare a crystalline adduct from 5-ethylbicyclo(2,2,1)-2-heptene and phenyl azide.

Investigation of the composition of the products boiling above 160°. The combined residues (total weight 616.2 g) boiling above tetrahydroindene (160°) obtained in different experiments were distilled from a Favorskii flask, and the distillate [b.p. 63° (21 mm) – 150° (6 mm), 435.7 g] was distilled in a column of 20 theoretical plates. Dicyclopentadiene and four hydrocarbons were separated in this distillation; the properties of these hydrocarbons are presented in the table.

2-Ethyl-1,4-endomethylenedecalin (XIII) was obtained by hydrogenation of (X) (3.0 g) in the cold in the presence of palladium black.

2-Ethyl-1,4-endomethylene-1,2,3,4-tetrahydronaphthalene (XIV) was obtained by dehydrogenation of (X) (5.0 g) by passing it four times over platinized carbon at 300-305°.

Synthesis of 2-vinyl-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene (X). A mixture of 28 g of 2-vinylbicyclo(2,2,1)-5-heptene and 16 g of butadiene was heated in an autoclave at 145-155° for 4.5 hr. Distillation of the reaction product gave 21.7 g of a mixture of vinylbicycloheptene and tetrahydroindene* and 3.8 g (10%) of 2-vinyl-1,4-endomethyleneoctahydronaphthalene.

B.p. 76-77° (1.5 mm), $n^{20}D$ 1.5140, d^{20}_4 0.9617, MR_D 54.53; calc. 54.70.

Found %: C 89.25, 89.34; H 10.40, 10.31. $C_{13}H_{18}$. Calculated %: C 89.58; H 10.39.

The hydrocarbon did not react with phenyl azide.

Synthesis of 2,3-(Δ^1-cyclopenteno-3,4)-1,4-endomethylene-1,2,3,4,5,5a,8,8a-octahydronaphthalene (XV). A mixture of 56.0 g of cyclopentadiene dimer with an m.p. of 30°, 22 g of butadiene, and 28 ml of benzene was heated in an autoclave at 150° for 4 hr. A total of 27.2 g of dicyclopentadiene was recovered by distillation of the reaction product, and 8.1 g of condensation product was obtained; b.p. 86-89° (1.5 mm), $n^{20}D$ 1.5363. The hydrocarbon partially crystallized when stored in a refrigerator. The solid part (3.3 g) had an m.p. of 35.5-36.5° (from alcohol). A mixture of this substance with cyclopenteno-1,4-endomethyleneoctahydronaphthalene obtained from the products of the condensation of cyclopentadiene with butadiene melted without depression of the melting point. The hydrocarbon did not react with phenyl azide. The yield was 4.5%, calculated on the dicyclopentadiene charged.

Found %: C 90.11, 90.20; H 9.70, 9.71. $C_{14}H_{18}$. Calculated %: C 90.28; H 9.72.

Attempts to separate an individual compound from the liquid part of the condensation product were unsuccessful.

*The tetrahydroindene was formed by isomerization of (I) [4].

SUMMARY

1. The condensation of cyclopentadiene with butadiene and the resulting codimers – 2-vinylbicyclo(2,2,1)-5-heptene and tetrahydroindene – have been studied.

2. It was shown that, depending on the temperature of the experiment, the condensation could be directed predominantly toward the formation of 2-vinylbicyclo(2,2,1)-5-heptene or of tetrahydroindene.

3. A number of products of higher molecular weight were separated, and the structures of 2-vinyl-1,4-endomethyleneoctahydronaphthalene and 2,5-(Δ^1-cyclopenteno-3,4)-1,4-endomethyleneoctahydronaphthalene were proved.

4. Judging from the composition of the high-molecular-weight condensation products, the double bond in the bicyclo(2,2,1)heptene structure is more active under the conditions of the Diels-Alder synthesis than is the vinyl double bond or the double bond in a six-membered or five-membered ring.

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CONDENSATION OF CYCLOPENTADIENE WITH ALIPHATIC DIENES

II. THE REACTION OF CYCLOPENTADIENE WITH ISOPRENE AND 2,3-DIMETHYL-1,3-BUTADIENE

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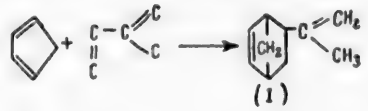
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3953-3959, December, 1960
Original article submitted January 14, 1960

In a continuation of our previous investigation [1], we have studied the condensation of cyclopentadiene with isoprene and 2,3-dimethyl-1,3-pentadiene.

The condensation of cyclopentadiene with isoprene is mentioned in one American patent [2], in which it is stated that the reaction proceeds at room temperature with the formation of 2-isopropenylbicyclo(2,2,1)-5-heptene (I), while 5-methyl-4,9,7,8-tetrahydroindene (II) is formed at 178-233°.



(I)

(II)

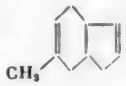
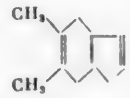
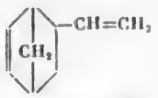
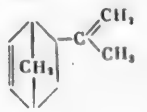
However, neither of the codimers was isolated, and their concentration in the reaction mixture was merely estimated by means of i.r. spectroscopy.

In an attempt to repeat the work described in the patent, it was found that at room temperature only an insignificant amount of condensation of cyclopentadiene with isoprene had occurred after 3.5 months, and the isopropenylbicycloheptene content of the reaction mixture did not exceed 2%, which made it impossible to isolate. When the condensation of cyclopentadiene with isoprene was carried out at 140-145°, i.e., under conditions optimum for the preparation of 2-vinylbicyclo-5-heptene [1], we were able to separate only 7% 2-isopropenylbicyclo(2,2,1)-5-heptene from the reaction products, and the second codimer – methyltetrahydroindene – was formed in extremely small amounts. With a further increase in the condensation temperature to 185-200°, the major product of the reaction was 5-methyltetrahydroindene, the yield of which reached 23%, and only traces of isopropenylbicycloheptene were formed.

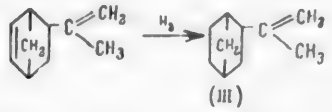
Thus, in the present case, as in the case of the condensation of cyclopentadiene with butadiene, the reaction can take place with the predominant formation of either of the codimers; under milder conditions, the cyclopentadiene acts as the diene component, while butadiene or isoprene acts as the diene under more vigorous conditions.

TABLE 1

Physical Properties of Codimers of Cyclopentadiene with Butadiene, Isoprene, and 2,3-Dimethylbutadiene

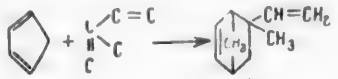
No.	Hydrocarbon	Boiling point (760 mm)	n_D^{20}	d^{20}_4
1		160°	1.4979	0.9261
2		181	1.4931	0.9099
3		199	1.4953	0.9080
4		140	1.4808	0.8884
5		169	1.4862	0.8999

The presence of two double bonds in compound (I)—one in the isopropenyl group and one in the bicycloheptene system—was confirmed by Raman spectroscopy* (lines due to the double bonds were 1644 cm^{-1} and 1572 cm^{-1}, respectively) [3]. It was also possible to confirm this structure by selective hydrogenation, since isopropenylbicycloheptene, in contrast to vinylbicycloheptene, adds only one mole of hydrogen; the more active disubstituted double bond in the bicycloheptene system hydrogenates in preference to the disubstituted double bond in the isopropenyl group.



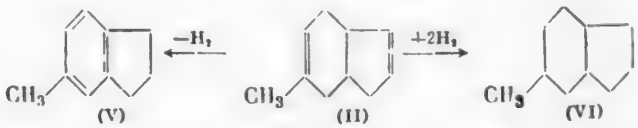
(III)

Had the condensation of cyclopentadiene with isoprene taken place in a manner such that 2-methyl-2-vinylbicyclo(2,2,1)-2-heptene (IV) was formed instead of isopropenylbicycloheptane, then by analogy to vinylbicycloheptene, selective hydrogenation would not have occurred.



(IV)

The structure of the second codimer—5-methyltetrahydroindene—was confirmed by dehydrogenation to 5-methylindane (V) and by hydrogenation to 5-methylhydrindane (VI).



(V) (II) (VI)

*The Raman study was carried out by V. T. Aleksanyan and Kh. E. Sterin in the laboratories of the Commission for Spectroscopy, Academy of Sciences of the USSR, for which we express our sincere appreciation.

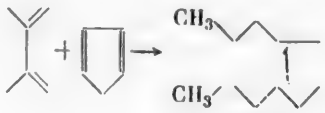
As in the case of the Raman spectrum of tetrahydroindene [1], the spectrum of 5-methyltetrahydroindene contained four, rather than two, lines in the region of double bond valence vibrations: 1603 (5), 1624 (4), 1665 (4), and 1683 (3) cm^{-1}.

It should be mentioned that separation of cyclopentadiene – isoprene codimers as individual compounds is more difficult than separation of cyclopentadiene – butadiene copolymers, since they have ten carbon atoms in the molecule, as do also isoprene dimers (the number of which can be as high as six) and cyclopentadiene dimers. Separation was accomplished by fractional distillation in a column of 100 theoretical plates.

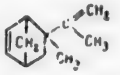
When 2,3-dimethyl-1,3-butadiene was used as the comonomer, it was found that it underwent practically no condensation with cyclopentadiene under mild conditions (145-150°), thereby contrasting with butadiene and isoprene. Under these conditions, 2,3-dimethylbutadiene polymerized slightly, but a large part of it did not react and could be recovered unchanged (about 60%); in this case, the major reaction of the cyclopentadiene was polymerization.

Thus, dimethylbutadiene, which has two substituted double bonds, is only slightly active as a dienophile.

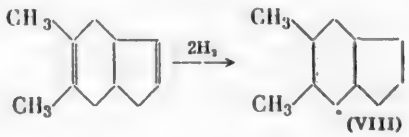
When the reaction was carried out under more vigorous conditions, 195-205°, 2,3-dimethyl-1,3-butadiene and cyclopentadiene gave 5,6-dimethyl-4,9,7,8-tetrahydroindene (VII) in a yield of 15%. In this case, the dimethylbutadiene acted as a diene, while the cyclopentadiene acted as the dienophile.



(VII)

The structure of the dimethyltetrahydroindene was confirmed by the following considerations. According to the analytical data, the product was a hydrocarbon having the composition $C_{11}H_{16}$, and, therefore, was a codimer of cyclopentadiene and dimethylbutadiene. Hence, it could have the structure  , 2-methyl-2-isopropenylbicyclo-5-heptene, or it could be dimethyltetrahydroindene (VII). Since the Raman spectrum of this hydrocarbon contained no lines characteristic of the vibration of a bicycloheptene double bond (about 1570 cm^{-1}) and also judging by the synthesis conditions and by its physical constants (the boiling point, $n^{20}D$ and d^{20}_4 for tetrahydroindene and its homologs are significantly higher than the corresponding constants for 2-vinylbicyclo-5-heptene and its homologs, see Table 1), the hydrocarbon was 5,6-dimethyl-4,9,7,8-tetrahydroindene.

Hydrogenation of the dimethyltetrahydroindene gave 5,6-dimethylhydrindane (VIII)



(VIII)

EXPERIMENTAL

The physical properties and analyses of all of the compounds prepared in the present work are shown in Table 2.

Condensation of cyclopentadiene with isoprene. a) To a 250-ml autoclave were charged 90.4 g of cyclopentadiene and 92.0 g of isoprene, and the mixture was heated at 140-145° for 3.5 hr. The reaction product (from five similar experiments) was distilled, first from a Favorskii flask (the fraction boiling at 60-66° at 21 mm) was collected), and then from a column with an efficiency of 30 theoretical plates (the fraction boiling at 55-66.8° at 20 mm with an $n^{20}D$ of from 1.4820 to 1.4988 was collected). The resulting distillate (101.1 g) was then distilled in a column of 100 theoretical plates. The distillation curve is shown in Fig. 1. Fractions 4, 5, and 6 were isoprene dimer; fractions 10-23 were 2-isopropenylbicyclo(2,2,1)-5-heptene (I). The yield of the latter was 6.8%, calculated on the isoprene charged.

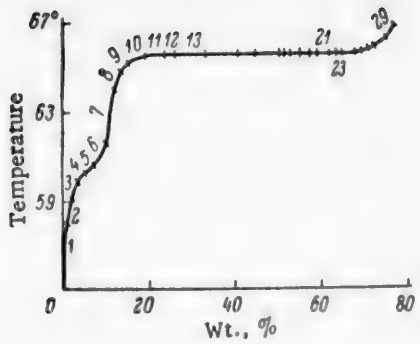


Fig. 1. Distillation curve for 2-isopropenylbicyclo(2,2,1)-5-heptene (pressure, 21 mm).

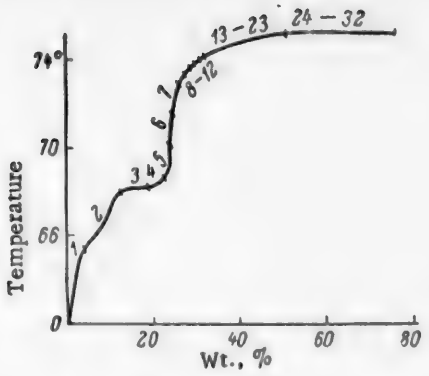


Fig. 2. Distillation curve for 5-methyltetrahydroindene (pressure, 21 mm).

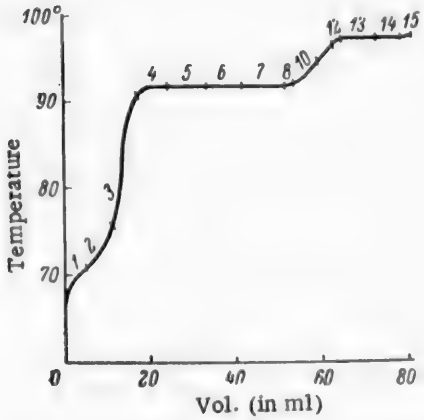


Fig. 3. Distillation curve for 5,6-dimethyltetrahydroindene (pressure, 24 mm).

b) To a 250-ml autoclave were charged 89 g of cyclopentadiene and 91 g of isoprene, and the mixture was heated at 185-200° for 2 hr. The reaction product was distilled first from a Favorskii flask, and the fraction boiling at 70-78° (22 mm) was collected. This distillate (from two experiments, 204.6 g) was then distilled in a column of 100 theoretical plates. The distillation curve is presented in Fig. 2.

Fractions 3 and 4 were cyclopentadiene dimer, fractions 8-12 were isoprene dimer (a mixture of m- and p-methylisopropenylcyclohexene), and fractions 13-23 were intermediate cuts prior to distillation of 5-methyltetrahydroindene. Fractions 24-32 were 5-methyltetrahydroindene; the yield was 23% calculated on the isoprene charged. The yields of cyclopentadiene dimer and of the mixture of m- and p-methylisopropenylcyclohexene were, respectively, 7 and 8%.

Complete hydrogenation of 5-methyltetrahydroindene and 5,6-dimethyltetrahydroindene was carried out in alcohol solution at ordinary temperatures in a bomb; the catalyst was platinum black. The resulting substance (VI) was chromatographed on silica gel and then distilled in a column; substance (VII) was distilled from a Favorskii flask.

Dehydrogenation of 5-methyltetrahydroindene (32.3 g) was carried out in a tubular reactor at 310-315° and at a space rate of 0.17; the catalyst was platinized carbon (15% Pt). The catalyzate was distilled in a column, and 23.4 g of 5-methylindane was obtained.

Condensation of cyclopentadiene with 2,3-dimethylbutadiene. The 2,3-dimethylbutadiene (b.p. 68.5-69.0°) was prepared from pinacol [7].

To a 250 ml autoclave were charged 57 g of cyclopentadiene, 71 g of dimethylbutadiene, and 0.1 g of hydroquinone, and the mixture was heated at 195-205° for 2 hr. Upon distillation of the product, 11% of the original dimethylbutadiene was recovered unchanged. The resulting distillate, boiling range 70-120° (20 mm) was redistilled in a column having an efficiency of 30 theoretical plates. The distillation curve is presented in Fig. 3.

Fractions 4-8 were 5,6-dimethyltetrahydroindene (VI); the yield was 15%, calculated on the 2,3-dimethylbutadiene reacted. Fractions 13-15 were dimethylbutadiene dimer

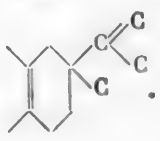


TABLE 2. Properties of Hydrocarbons Obtained from Condensation of Cyclopentadiene with Isoprene and 2,3-Dimethyl-1, 3-butadiene and the Products of Hydrogenation and Dehydrogenation

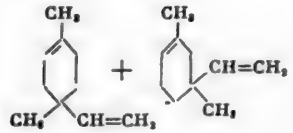
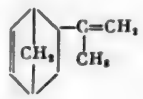
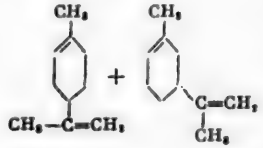
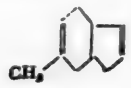
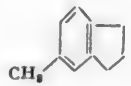
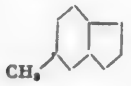
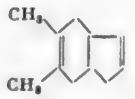
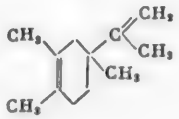
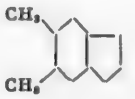
No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Empirical formula	Found (%) C	Found (%) H	Calc. (%) C	Calc. (%) H	Literature data
1		60.3—60.4° (21)	1.4668	—	—	—	$C_{10}H_{16}$	—	—	—	—	B. p. 62.0—62.5° (26mm), n_D^{20} 1.4654[4]
2		65.6 (21), 169 (760)	1.4862	0.8999	42.83	43.04	$C_{10}H_{14}$	89.75, 89.49	10.47, 10.41	89.48	10.51	—
3		73.1—74.2 (21)	1.4733	—	—	—	$C_{10}H_{16}$	—	—	—	—	B. p. 74° (26mm), n_D^{20} 1.4735 [4]
4		75.2—75.3 (21)	1.4931	0.9099	42.88	43.04	$C_{10}H_{14}$	89.47, 89.50	10.48, 10.45	89.48	10.51	

TABLE 2 (Cont'd)

No.	Compound	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Empirical formula	Found (%) C	Found (%) H	Calc. (%) C	Calc. (%) H	Literature data
5		91.5°(20), 204 (760)	1.5329	0.9464	43.35	42.58	$C_{10}H_{12}$	—	—	—	—	B.p. 201.1° (740.5 mm) $n^{25}D$ 1.5311, d^{25}_4 0.9442 [5]
6		79.8 (25), 183 (760)	1.4661	0.8683	44.11	43.98	$C_{10}H_{18}$	86.95, 87.15	13.15, 13.06	86.88	13.12	
7		92.1 (24), 199 (760)	1.4953	0.9080	47.64	47.66	$C_{11}H_{16}$	88.91, 88.87	10.95, 10.95	89.12	10.88	—
8		97.8 (24), 205 (760)	1.4811	—	—	—	$C_{12}H_{20}$	—	—	—	—	B.p. 205° (750 mm), 85° (13 mm), $n^{20}D$ 1.48074; B.p. 205-206° (738 mm) $n^{20}D$ 1.4810 [6]
9		70.7 (7), 203 (760)	1.4723	0.8774	48.62	48.60	$C_{11}H_{20}$	86.72, 86.88	13.20, 13.20	86.76	13.24	

SUMMARY

1. The Diels-Alder condensation of cyclopentadiene with isoprene and the resulting codimers – 2-isopropenylbicyclo(2,2,1)-5-heptene and 5-methyl-4,9,7,8-tetrahydroindene were studied.

2. It was found that, depending on the reaction temperature, the condensation of cyclopentadiene with isoprene can take place with the formation of predominantly either 2-isopropenylbicyclo-5-heptene or 5-methyltetrahydroindene.

3. 2,3-Dimethylbutadiene reacts with cyclopentadiene only as a diene under comparatively mild conditions (200°) with the formation of 5,6-dimethyl-4,9,7,8-tetrahydroindene.

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THE ACTION OF SODIUM THIOPHENOLATE ON 1,1,1-TRICHLOROPENTANE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3960-3964, December, 1960
Original article submitted February 4, 1960

It has previously been established that the action of nucleophilic reagents on 1,1,1-trichloroalkanes, RCH_2CCl_3, does not result in replacement of the chlorine atoms of the trichloromethyl group; rather, elimination of hydrogen chloride takes place, to a greater or lesser extent depending on the basicity of the reagent and on the reaction conditions, with the formation of 1,1-dichloro-1-alkenes, which, in turn, can undergo further reaction. In this connection, it seemed of interest to study the action of sodium thiophenolate on 1,1,1-trichloroalkanes, for sodium thiophenolate is a highly nucleophilic reagent with a low basicity [3]. The action of sodium thiophenolate on 1,1,1-trichloroethane has previously been investigated [4], and it was reported that $CH_3C(SC_6H_5)_3$ is formed. However, it was later shown [5] that the compound formed in this reaction is actually $C_6H_5SCH_2CH_2SC_6H_5$. Since this compound could be formed from 1,2-dichloroethane present as an impurity in the 1,1,1-trichloroethane [6], the reaction was carried out with pure 1,1,1-trichloroethane and sodium phenolate in an excess of aqueous base, and it was found that the only reaction products are $C_6H_5SCH_2CH_2SC_6H_5$ and $(C_6H_5)_2S_2$. The present work was devoted to a study of the action of sodium thiophenolate on 1,1,1-trichloropentane, and it was shown that this reaction leads to a more complex mixture of products than that described previously. The 1,1,1-trichloropentane used in this work was prepared by telomerization of ethylene and chloroform [7], and it contained no impurities. No reaction was detected when an alcoholic solution of 1,1,1-trichloropentane and sodium thiophenolate (in a mole ratio of 1 : 4) was heated at the boiling point of the alcohol for a number of hours. When these two reagents were heated in an autoclave at 165-175° for 15 hr, a mixture of products containing sulfur but no chlorine was obtained in addition to a large amount of diphenyl sulfide. The amount of diphenyl sulfide obtained corresponded approximately to the following equation:

$$C_3H_7CH_2CCl_3 + 2C_6H_5SNa \longrightarrow (C_6H_5)_2S_2.$$

Three compounds containing one, two, and three thiophenol groups, respectively, were separated from the mixture of products. The compound containing one thiophenol group had the composition $C_{11}H_{14}S$, and, consequently, it could be $C_3H_7CH = CHSC_6H_5$ or the isomeric $C_3H_7C(SC_6H_5) = CH_2$. When this compound was heated in a mixture of hydrochloric and acetic acids, thiophenol was produced, and treatment with 2,4-dinitrophenylhydrazine in an acid medium gave n-valeraldehyde 2,4-dinitrophenylhydrazone and thiophenol. This proves that the structure of the compound is $C_3H_7CH = CHSC_6H_5$. The compound containing two thiophenol groups had the composition $C_{17}H_{20}S_2$ (when oxidized, it gave a disulfone having the composition $C_{17}H_{20}O_4S_2$), and it could be one of three compounds: $C_3H_7CH(SC_6H_5)CH_2SC_6H_5$, $C_3H_7CH_2CH(SC_6H_5)_2$, or $C_3H_7C(SC_6H_5)_2CH_3$. This compound apparently was $C_3H_7CH(SC_6H_5)CH_2SC_6H_5$, since it was not hydrolyzed by a boiling mixture of hydrochloric and acetic acids, and no hydrazone was formed when it was subjected to the action of 2,4-dinitrophenylhydrazine in acid medium; hence, the last two compounds may be eliminated. The third substance, which contained three thiophenol groups, had the composition $C_{23}H_{24}S_3$. On the basis of this composition, it could be one of three possible compounds:

$$C_3H_7CH_2C(SC_6H_5)_3,\ C_3H_7CH(SC_6H_5)CH(SC_6H_5)_2,\ C_3H_7C(SC_6H_5)_2CH_2SC_6H_5.$$

When heated with a mixture of hydrochloric and acetic acids, it hydrolyzed with the formation of thiophenol and a compound of the composition $C_{11}H_{14}OS$, which formed a 2,4-dinitrophenylhydrazone. This same 2,4-dinitrophenylhydrazone was formed directly by the treatment of the compound $C_{23}H_{24}S_3$ with 2,4-dinitrophenylhydrazine in an acid medium. The formation of a carbonyl compound during hydrolysis eliminates the compound $C_3H_7CH_2C(SC_6H_5)_3$ from consideration, since hydrolysis of a compound having such a structure should yield thiophenol and valeraldehyde. That the carbonyl compound of the composition $C_{11}H_{14}OS$ was 1-phenylmercapto-2-pentanone was proved by direct synthesis from 1-chloro-2-pentanone and sodium thiophenolate:

$$CH_3CH_2CH_2COCH_2Cl + C_6H_5SNa \longrightarrow CH_3CH_2CH_2COCH_2SC_6H_5.$$

Consequently, on the basis of these data, the compound was $C_3H_7C(SC_6H_5)_2CH_2SC_6H_5$. Therefore, the reaction of 1,1,1-trichloropentane with sodium thiophenolate takes place according to:

$$C_3H_7CH_2CCl_3 + C_6H_5SNa \longrightarrow C_3H_7CH_2{=}CHSC_6H_5 +$$
$$+ C_3H_7CH(SC_6H_5)CH_2SC_6H_5 + C_3H_7C(SC_6H_5)_2CH_2SC_6H_5 + (C_6H_5)_2S_2.$$

These results show that this reaction does not proceed with replacement of the chlorine atoms in the CCl_3 group by thiophenol groups; rather, the CCl_3 group is reduced (the sodium thiophenolate is concurrently oxidized to diphenyl sulfide), and this is followed by further conversion of the reduction products. It is difficult to say, on the basis of the structures of the products obtained, just which compound is formed by direct reduction of the 1,1,1-trichloropentane during the course of the reaction. It might be assumed that the 1-phenylmercapto-1-pentene is formed from 1-chloro-1-pentene or 1-pentene, and the same might be said of the 1,2-bis(phenylmercapto)pentane. Hence, there is another possible course of the reaction, namely, the 1,1,1-trichloropentane is dehydrochlorinated by the sodium thiophenolate to 1,1-dichloro-1-pentene, which undergoes further reduction to 1-pentene* or 1-chloro-1-pentene, and these subsequently react with more sodium thiophenolate to give the products indicated. Therefore, the reaction of 1,1-dichloro-1-pentene with sodium thiophenolate was studied. When 1,1-dichloro-1-pentene was heated with an excess of sodium thiophenolate in alcohol solution at 160-170°, a small amount of diphenyl sulfide and two sulfur-containing compounds were formed. One of the latter two compounds proved to be $C_3H_7CH = CHSC_6H_5$ (only a small amount was obtained), while the other, which was the major product of the reaction, was $C_3H_7C(SC_6H_5) = CHSC_6H_5$. Thus, the reaction of 1,1-dichloro-1-pentene with sodium thiophenolate proceeds according to:

$$C_3H_7CH{=}CCl_2 + C_6H_5SNa \longrightarrow C_3H_7CH{=}CHSC_6H_5 +$$
$$+ C_3H_7C(SC_6H_5){=}CHSC_6H_5 + (C_6H_5)_2S_2.$$

The structure of the phenylpentenyl sulfide was proved by its reaction with 2,4-dinitrophenylhydrazine in acid medium, which yielded valeraldehyde 2,4-dinitrophenylhydrazone and thiophenol. The structure of the 1,2-bis(phenylmercapto)-1-pentene was proved by hydrolysis with a mixture of hydrochloric and acetic acids to 1-phenylmercapto-2-pentanone and thiophenol.

$$C_3H_7C(SC_6H_5){=}CHSC_6H_5 \xrightarrow[H_2O]{H^+} C_3H_7COCH_2SC_6H_5 + C_6H_5SH.$$

This result indicates that the interaction of 1,1,1-trichloropentane with thiophenol does not take place by dehydrochlorination to 1,1-dichloro-1-pentene (if this reaction does occur, it does so to an insignificant extent) and that the first stage of the basic reaction is reduction of the trichloromethyl group. However, the mechanism is still obscure, and further study is necessary. It may be remarked that the reaction studied in the present work, the interaction of 1,1-dichloro-1-pentene with sodium thiophenolate, proceeds somewhat differently than the reaction of 1,1-dichloro-1-hexene [9] and 1,1-dichloro-1-pentene with sodium ethylmercaptide [2], reactions which we studied previously. Reduction of the 1,1-dichloro-1-alkene and formation of products having the structure $RCH = CHSC_2H_5$ were not observed in the latter case.

EXPERIMENTAL

The action of sodium thiophenolate on 1,1,1-trichloropentane. A solution of 35 g of 1,1,1-trichloropentane and the sodium thiophenolate (prepared from 90 g of thiophenol) in 250 ml of alcohol was heated in an

*According to the data reported in reference [8], the interaction of 1,1-dibromo-1-propene with sodium ethylmercaptide leads to methylacetylene.

autoclave at 165-175° for 15 hr. When the reaction was complete, water was added, and the reaction products were extracted with chloroform. The chloroform extract was dried over potassium carbonate and the chloroform was distilled; the residue crystallized on cooling. The crystals (diphenyl sulfide) were separated by filtration and washed on the filter with cold petroleum ether. The filtrate was distilled under vacuum. Four fractions were collected: first fraction, boiling range 90-130° (1 mm), 9.2 g; second fraction, boiling range 130-160° (1 mm), 11.9 g; third fraction, boiling range 160-210° (1 mm), 18.4 g; fourth fraction, boiling range 210-240° (1 mm),8 g. A second vacuum distillation of the first fraction yielded 7.8 g of 1-phenylmercapto-1-pentene.

B.p. 94.5-95.5° (1 mm), $n^{20}D$ 1.5648, d^{20}_4 1.0051.

Found %: C 74.14, 73.91; H 7.66, 7.74; S 17.78, 17.60. $C_{11}H_{14}S$. Calculated %: C 74.15; H 7.86; S 17.97.

Thiophenol was obtained by heating a solution of the 1-phenylmercapto-1-pentene in a mixture of hydrochloric and acetic acids. The reaction of an alcohol solution of the compound with 2,4-dinitrophenylhydrazine in the presence of sulfuric acid gave valeraldehyde thiophenol and 2,4-dinitrophenylhydrazone with an m.p. of 106-107° (from alcohol); a mixture of this hydrazone with a known sample of valeraldehyde 2,4-dinitrophenylhydrazone showed no depression of the melting point. Oxidation of the 1-phenylmercapto-1-pentene with hydrogen peroxide in acetic acid gave 1-phenylsulfonyl-1-pentene, m.p. 97-98° (from petroleum ether).

Found %: C 62.62, 62.54; H 6.57, 6.56; S 15.00, 14.90. $C_{11}H_{14}O_2S$. Calculated %: C 62.86; H 6.66; S 15.23.

The second fraction was diphenyl sulfide. The total amount of diphenyl sulfide separated after the reaction was 35.1 g.

The third fraction was treated as follows: In order to separate any unsaturated sulfides which might be present, the fraction was refluxed for 5 hr with a mixture of hydrochloric and acetic acids. Since no thiophenol was formed, zinc dust was added to the solution to reduce any traces of diphenyl sulfide to thiophenol. Subsequent treatment following these operations yielded 11.6 g of 1,2-bis(phenylmercapto)pentane.

B.p. 168-170° (1 mm), $n^{20}D$ 1.5994, d^{20}_4 1.0822.

Found %: C 70.56, 70.76; H 6.94, 7.02; S 22.21, 22.01. $C_{17}H_{20}S_2$. Calculated %: C 70.79; H 6.91; S 22.22.

Oxidation of this compound with hydrogen peroxide in acetic acid gave 1,2-bis(phenylsulfonyl)pentane, m.p. 99-100° (from alcohol).

Found %: C 57.78, 57.89; H 5.70, 5.60; S 17.99, 18.03. $C_{17}H_{20}O_4S_2$. Calculated %: C 57.95; H 5.68; S 18. 18.

A second distillation of the fourth fraction separated 5.4 g of 1,2,2-tri(phenylmercapto)pentane, b.p. 231-233° (1.5 mm), d^{20}_4 1.1490.

Found %: C 69.89, 69.77; H 5.92, 6.01; S 23.91, 23.83. $C_{23}H_{24}S_3$. Calculated %: C 69.94; H 6.06; S 24.24.

The action of 2,4-dinitrophenylhydrazine on an alcohol solution of the compound in the presence of sulfuric acid lead to thiophenol and 1-phenylmercapto-2-pentanone 2,4-dinitrophenylhydrazone, m.p. 104-105° (from alcohol).

Found %: N 15.12, 14.93. $C_{17}H_{18}O_4N_4S$. Calculated %: N 14.97.

When a solution of 1,2,2-tri(phenylmercapto)pentane in a mixture of hydrochloric and acetic acids was heated for 3 hr, thiophenol was obtained along with 1 phenylmercapto-2-pentanone, b.p. 116-117° (2 mm), $n^{20}D$ 1.5580, d^{20}_4 1.0761.

Found %: C 67.83, 68.06; H 7.12, 7.16; S 17.04, 16.94. $C_{11}H_{14}OS$. Calculated %: C 68.04; H 7.21; S 16.49.

This ketone gave a 2,4-dinitrophenylhydrazone with an m.p. of 104-105° (from alcohol).

1-Phenylmercapto-2-pentanone. To a solution of sodium thiophenolate (from 7 g of thiophenol) in alcohol was added 6 g of 1-chloro-2-pentanone. The reaction was exothermic. The solution was heated for 15 min, poured into water, and extracted with chloroform. There was obtained 6.1 g of 1-phenylmercapto-2-pentanone, b.p. 119-120° (2.5 mm), $n^{20}D$ 1.5570, d^{20}_4 1.0756. The 2,4-dinitrophenylhydrazone, which melted at 104-105° (from alcohol), caused no depression of the melting point when mixed with a sample of the 2,4-dinitrophenylhydrazone from the preceding experiment.

The action of sodium thiophenolate on 1,1-dichloro-1-pentene. A solution of 20 g of 1,1-dichloro-1-pentene and sodium thiophenolate (from 45.2 g of thiophenol and 9.5 g of sodium) in 120 ml of alcohol was heated in an autoclave at 160-170° for 18 hr. The reaction mixture was diluted with water, and the oil which separated was extracted with ether. The ether extract was washed with a base and dried over potassium carbonate. Vacuum distillation resulted in 3.2 g of 1-phenylmercapto-1-pentene [b.p. 94-95° (1 mm), $n^{20}D$ 1.5646, d^{20}_4 1.0050], 5 g of diphenyl sulfide, and 22.1 g of 1,2-bis(phenylmercapto)-1-pentene with a b.p. of 172-173° (1 mm), $n^{20}D$ 1.6340, d^{20}_4 1.1111.

Found %: C 71.28, 71.35; H 6.31, 6.21; S 22.42, 22.59. $C_{17}H_{18}S_2$. Calculated %: C 71.33; H 6.29; S 22.33.

The action of an alcoholic solution of 2,4-dinitrophenylhydrazine on the 1-phenylmercapto-1-pentene in the presence of sulfuric acid gave valeraldehyde 2,4-dinitrophenylhydrazone, m.p. 106-107°, which caused no depression of the melting point when mixed with a known sample of the hydrazone. When a solution of 1,2-bis-(phenylmercapto)-1-pentene in a mixture of hydrochloric and acetic acids was heated, thiophenol was obtained along with 1-phenylmercapto-2-pentanone, b.p. 119-120° (2.5 mm), $n^{20}D$ 1.5570, d^{20}_4 1.0743. The 2,4-dinitrophenylhydrazone had an m.p. of 104-105° (from alcohol), and caused no depression of the melting point when mixed with a known sample of the hydrazone.

SUMMARY

1. It was shown that the reaction of 1,1,1-trichloropentane with sodium thiophenolate gives diphenyl sulfide, 1-phenylmercapto-1-pentene, 1,2-bis(phenylmercapto)pentane, and 1,2,2-tri(phenylmercapto)pentane. It is proposed that the first stage of this reaction is reduction of the trichloromethyl group.

2. It was found that the major product of the reaction of 1,1-dichloro-1-pentene with sodium thiophenolate is 1,2-bis(phenylmercapto)-1-pentene, and smaller amounts of 1-phenylmercapto-1-pentene and diphenyl sulfide are also formed.

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AUTOOXIDATION OF 4-SEC-BUTYL-o-XYLENE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3964-3967, December, 1960
Original article submitted January 11, 1960

In a continuation of our previous investigations [1], we have studied in the present work the autooxidation of 4-sec-butyl-o-xylene (I) by atmospheric oxygen at 110° in the presence of manganese resinate in combination with some or all of $Ca(OH)_2$, NaOH, Na_2CO_3, sodium stearate, and cobalt acetate. The oxidation was carried out until the maximum concentration of hydroperoxides was obtained or until hydroperoxide had completely disappeared from the reaction mixture. It was found that the maximum concentration of hydroperoxide depends on the nature of the promoter and the amount of manganese resinate. The highest concentration of hydroperoxide (13%) was formed during autooxidation of (I) in the presence of manganese resinate and sodium carbonate. When 4-sec-butyl-o-xylene was oxidized until hydroperoxide completely disappeared from the reaction mixture, the following products were formed: 3,4-dimethylacetophenone (II), o-xylenol (1,2,4) (III), 1,2-dimethylphenylmethylethylcarbinol (IV), 2-methyl-4-sec-butyl- and 2-methyl-5-sec-butylbenzoic acids (V), and 2-methyl-4-sec-butyl- and 2-methyl-5-sec-butylbenzyl alcohols (VI). Oxidation of hydrocarbon (I) occurred to the extent of 25.8% when the oxidation was carried out in the presence of manganese resinate, sodium stearate, and calcium hydroxide over a period of 60 hr and at an air rate of 18 liters/hr. Products (II to VI) were formed in a molar relationship of 3.75 : : 1 : 3 : 5.65 : 2.5, respectively. When (I) was oxidized in the presence of manganese resinate, cobalt acetate, sodium stearate, sodium hydroxide, and calcium hydroxide over the same period of time and with the same air feed rate, oxidation amounted to 32.3%, and products (II to VI) were obtained in a molar relationship of 7.5 : 1 : : 3 : 26 : 4, respectively. On the basis of the composition of the oxidation products it can be said that in the oxidation of 4-sec-butyl-o-xylene, the oxygen attacks all three radicals with the formation of a mixture of hydroperoxides: 2-methyl-4-sec-butylbenzyl (VII), 2-methyl-5-sec butylbenzyl (VIII), and 3,4-dimethyl- α-methyl-α-ethylbenzyl (IX). (The presence of these hydroperoxides was confirmed by oxidation to the corresponding alcohols.) The secondary butyl radical is oxidized twice as fast as the methyl radical in the presence of manganese resinate, sodium stearate, and calcium hydroxide. When cobalt acetate is added to the initiator, the methyl group is oxidized 1.3 times as fast.

The value of the ratio of 2-methyl-4-sec-butylbenzoic acid to 2-methyl-5-sec-butylbenzoic acid shows that of the two methyl groups, the one most subject to oxidation is the one which is in the para position to the secondary butyl radical (it is attacked approximately 1.3 times as fast).

EXPERIMENTAL

The 4-sec-butyl-o-xylene (I) was prepared by alkylation of o-xylene with 2-butene in the presence of a $BF_3 \cdot H_3PO_4$ catalyst; the mole ratio of xylene to butene to catalyst was 2 : 1 : 0.2, the temperature was 60°, and the 2-butene feed rate was 2 liters/hr/mole. The average yield was 90%. Prior to oxidation, the butylxylene was washed several times with concentrated sulfuric acid, washed with a 10% aqueous solution of sodium hydroxide and with water, dried over solid sodium hydroxide, and distilled over metallic sodium. The b.p. was 212-213°, $n^{20}D$ 1.5020, d^{20}_4 0.8724. Oxidation of the butylxylene with nitric acid in an autoclave converted it to trimellitic acid, m.p. 224-228°. The literature [2] reports an m.p. of 229-230°.

TABLE 1

Expt. No.	Amount charged: 4-sec butyl o-xylene (in g)	Amount charged: manganese resinate (in mg)	Promoter (in mg)		Max. hydroperoxide conc., %	Time to formation of max hydroperoxide conc. (in hr)
1	32.4	2	$Ca(OH)_2$	200	8.3	6
2	32.4	1.2	NaOH	40	8.0	8
3	115	3.0	NaOH $Ca(OH)_2$	200 100	7.6	18
4	140	20	$Ca(OH)_2$	2000	3.8	2
5	140	8	Na_2CO_3	1000	13.1	11
6	20	0.8	Na_2CO_3	150	12.0	11
7	40	1.2	Sodium stearate $Ca(OH)_2$	50 250	7.7	6
8	100	4	Sodium stearate $Ca(OH)_2$	60 1000	9.5	5
9	140	1	Sodium stearate Cobalt acetate $Ca(OH)_2$ NaOH	500 150 300 100	0.6	10

TABLE 2. Effect of Oxidation Conditions on the Composition of the Products of Hydroperoxide Decomposition

Expt. No.	Amt. of catalyst per mole of hydrocarbon (mg)		Oxidation time, hr	Max. percent hydroperoxide	Yield of oxidation products (in %)* (II)	(III)	(IV)	(V)	(VI)
1	Manganese resinate Cobalt acetate Sodium stearate $Ca(OH)_2$ NaOH	1 150 500 300 100	60	0.6	18.1 4.8	2.4 1.6	7.5 2.1	62.3 17.3	9.7 2.7
2	The same		35	0.8	18.2 6.1	—	15.6 5.3	56.2 18.9	10.0 3.4
3	Manganese resinate Sodium stearate $Ca(OH)_2$	5 100 1	60	10.5	23.7 5.4	6.3 1.4	18.8 4.3	35.6 8.1	15.6 3.5

*The upper figure is the yield in mole %, and the lower is the yield in percent of theoretical.

Autooxidation of 4-sec-butyl-o-xylene. The autooxidation was carried out in the manner described previously [1] at 110° and with an air feed rate of 18 liters/hr/mole until maximum hydroperoxide concentration was obtained or until hydroperoxide completely disappeared from the reaction mixture.

Data from the experiments in which oxidation was continued to maximum hydroperoxide concentration in the reaction mixture are presented in Table 1.

Reduction of the hydroperoxides. To a three-neck flask fitted with a stirrer and reflux condenser was charged 93.9 g of the reaction mixture, which contained 8.5% hydroperoxide. A saturated aqueous solution of 8 g of Na_2SO_3 was added, and the mixture was heated on a water bath until a negative test for hydroperoxide was

obtained. The aqueous layer was then separated from the hydrocarbon layer, and the acid was extracted from the latter with a solution of sodium carbonate. A total of 1.7 g (1.4%) of 2-methyl-4-sec-butyl- and 2-methyl-5-sec-butylbenzoic acids (V) was obtained. After the sodium carbonate extraction, the hydrocarbon layer was treated with 10% alkali to extract phenols (none were found), washed with water, dried, and distilled. The distillation gave 76.5 g of unoxidized hydrocarbon, 8 g of a fraction boiling in the range of 90-150° (2 mm), and 1.7 g of tar. The fraction boiling at 90-150° (2 mm) contained (II), (IV), and (VI). The yields of these compounds were 1.2, 3.4, and 2.4%, respectively.

Oxidation of (I) to the complete disappearance of hydroperoxide from the reaction mixture was carried out in the same manner as described above with the one exception that after maximum hydroperoxide concentration had been reached, the air flow was continued for an additional time. Treatment of the reaction mixture was carried out in a manner analogous to that described above. The yields of oxidation products at different times and in the presence of different catalyst mixtures are presented in Table 2.

Characterization of the Oxidation Products

3,4-Dimethylacetophenone (II). This compound was identified as the 2,4-dinitrophenylhydrazone with an m.p. of 250-251° (from toluene) and as the oxime with an m.p. of 86.5-87.5° (from alcohol) [3].

The amount of (II) was determined by oxime formation [4].

o-Xylenol (1,2,4) (III). This material was obtained in the form of small colorless needles, m.p. 63.5-64° (from petroleum ether). It was converted to 1,2-dimethylphenoxyacetic acid, m.p. 160-161°.

The literature reports an m.p. of 62.5° for o-xylenol (1,2,4) [5] and an m.p. of 163° for 1,2-dimethylphenoxyacetic acid [6].

1,2-Dimethylphenylmethylethylcarbinol (IV). This compound was determined quantitatively by dehydration with potassium bisulfate in a diisopropylbenzene medium and subsequent titration of the water formed by means of Fischer's reagent [7].

The total primary alcohols (VI) were determined by acetylation with 12% aqueous acetic anhydride in pyridine [8].

The 2-methyl-4-sec-butyl- and 2-methyl-5-sec-butylbenzoic acids (V) were separated as a viscous yellow oil which boiled in the limits of 153-156° (2 mm). The structures and the ratio of these two compounds were determined by decarboxylation in quinoline over copper powder and subsequent oxidation of the resulting dialkylbenzenes to phthalic acids with 10% NHO_3 in an autoclave. The terephthalic acid was separated from the isophthalic acid by solution of the latter in water at 80°. The dimethyl esters of these acids were prepared. The dimethyl terephthalate melted at 140-141° and the dimethyl isophthalate melted at 66-67°; both of these are in agreement with the literature values.

SUMMARY

1. Autooxidation of 4-sec-butyl-o-xylene by atmospheric oxygen at 110° was studied in the presence of manganese resinate, calcium hydroxide, sodium stearate, cobalt acetate, sodium carbonate, and NaOH.

2. It was found that all three alkyl radicals undergo oxidation, and the rate of oxidation depends on the nature of the promoter. Of the two methyl groups, the one in the para position to the secondary butyl radical was more easily oxidized.

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SULFONATION OF β-DIKETONES

XII. SULFONATION OF 2 PHENYL-1,3-INDANEDIONE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3967-3972, December, 1960
Original article submitted January 25, 1960

β-Diketones may be sulfonated at the active methylene group by dioxane-sulfur trioxide [1] or by a mixture of sulfuric acid and acetic anhydride [2].

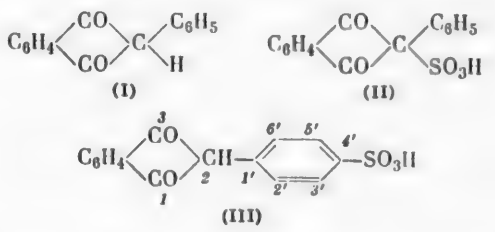
The aim of the present work was to determine the effect of the solvent, the sulfonating agent, and the temperature on the sulfonation of 2-phenyl-1,3-indanedione (I). The sulfonating agents used in this work were chlorosulfonic acid and a mixture of concentrated sulfuric acid and acetic anhydride; solvents were 1,2-dichloroethane, chloroform, carbon tetrachloride, isooctane, dioxane, and diethyl ether.

In all cases, the use of the mixture of sulfuric acid and acetic anhydride as the sulfonating agent resulted in the formation of 2-phenyl-1,3-indanedione-2-sulfonic acid (II) (Table 1).

A series of salts of this acid were prepared (Table 2).

The salts were prepared by neutralization of an aqueous solution of the acid with the appropriate metal carbonate or hydroxide. If the sulfonate was highly soluble, the chloride or nitrate of the same metal was used to salt out the product. The less soluble sulfonates could also be prepared by ion exchange between the appropriate metal salt and the sodium sulfonate. The majority of the salts were readily soluble in water. The less soluble sulfonates were those of potassium, rubidium, strontium, barium, and lead. In the presence of pyridine, the cobalt, nickel, and manganese sulfonates formed pyridine-containing complex salts; these will be considered in a separate communication.

There has been but little study of the interaction of chlorosulfonic acid and β-diketones [2]. Sulfonation of 2-phenyl-1,3-indanedione with chlorosulfonic acid in dioxane or in diethyl ether gave the same sulfonic acid (II), while when the reaction medium was 1,2-dichloroethane, chloroform, carbon tetrachloride, or isooctane, the phenyl group of 2-phenyl-1,3-indanedione was sulfonated in the para position, and 2-phenyl-1,3-indanedione-4'-sulfonic acid was obtained (III).



(I) (II) (III)

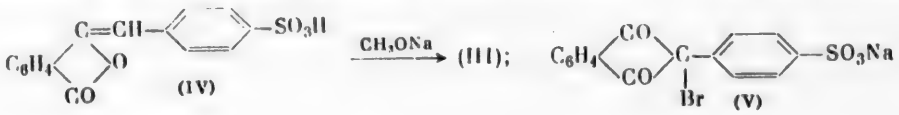
The structure of acid (III) was proved by alkaline cleavage, which yielded phthalic acid and p-toluenesulfonic acid; the latter was identified by conversion to the anilide.

TABLE 1

Sulfonation of 2-Phenyl-1,3-indanedione

Solvent	Sulfonating agent	Ratio of 2-phenyl-1,3-indanedione to sulfonating agent (in moles)	Yield of 2-phenyl-1,3-indanedione-2-sulfonic acid (in %)	Yield of 2-phenyl-1,3-indanedione-4-sulfonic acid (in %)
1,2-Dichloroethane	$ClSO_2OH$	1 : 1	—	31
		1 : 2	—	38
		1 : 3	—	46
		1 : 4	—	51
		1 : 5	—	50
	$H_2SO_4 + (CH_3CO)_2O$	1 : 1	45	—
		1 : 2	56	—
		1 : 1.3	77	—
Chloroform	$ClSO_2OH$	1 : 1	—	28
		1 : 2	—	42
		1 : 3	—	45
	$H_2SO_4 + (CH_3CO)_2O$	1 : 1	40	—
		1 : 2	50	—
Carbon tetrachloride	$ClSO_2OH$	1 : 1	—	33
		1 : 2	—	45
	$H_2SO_4 + (CH_3CO)_2O$	1 : 1	38	—
		1 : 2	42	—
Isooctane	$ClSO_2OH$	1 : 1	—	30
		1 : 2	—	45
Dioxane	$ClSO_2OH$	1 : 1	40	—
		1 : 2	52	—
	$H_2SO_4 + (CH_3CO)_2O$	1 : 1	35	—
		1 : 2	49	—
Diethyl ether	$ClSO_2OH$	1 : 1	12	—
		1 : 2	19	—

It is well known that 2-phenyl-1,3-indanedione can be prepared by sodium methylate-catalyzed isomerization of benzalphthalide. In order to prepare acid (III) by this method, benzalphthalide was sulfonated, and the resulting sulfonic acid (IV) was rearranged by means of sodium methylate. This route gave the same acid (III).



2-Phenyl-1,3-indanedione-4' sulfonic acid contains an active hydrogen in the 2 position which is readily replaced by bromine, and the sodium and potassium salts of 2-bromo 2-phenyl-1,3-indanedione 4'-sulfonic acid (V) were prepared in good yields. As in other bromoindanediones, the bromine atom is not strongly bonded and is readily split off. The compound interacts with water, splitting out hypobromous acid, and with aniline it gives the aniline salt of 2-anilino-2-phenyl-1,3-indanedione-4'-sulfonic acid (VI), which was obtained in the form of yellow crystals.

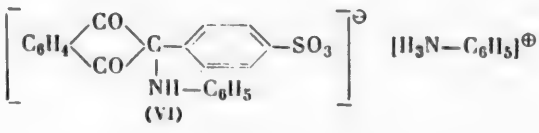


TABLE 2

Salts of 2-Phenyl-1,3-indanedione-2-sulfonic Acid

No.	Name of salt and empirical formula	Found (%)		Calc.(%)	Notes
1	Sodium salt $C_{15}H_9O_5SNa$	Na	6.81	7.08	Poorly developed prisms
	$C_{15}H_9O_5SNa \cdot 3H_2O$	Na H_2O	5.87 14.21	6.08 14.29	Lamellar crystals
2	Potassium salt $C_{15}H_9O_5SK$	K	11.25	11.40	Long fine prisms
3	Rubidium salt $C_{15}H_9O_5SRb$	Rb	21.72	22.10	Prismatic crystals
4	Silver salt $C_{15}H_9O_5SAg \cdot H_2O$	Ag H_2O	24.70 4.70	25.25 4.22	Small hexagonal plates and prisms
5	Thallium salt $C_{15}H_9O_5STl$	Tl	40.49	40.41	Long prisms
6	Magnesium salt $(C_{15}H_9O_5S)_2Mg \cdot 2H_2O$	Mg H_2O	3.53 5.32	3.67 5.43	Poorly developed plates
7	Calcium salt $(C_{15}H_9O_5S)_2Ca \cdot 6H_2O$	Ca H_2O	5.32 13.89	5.34 14.40	Lamellar crystals
8	Strontium salt $(C_{15}H_9O_5S)_2Sr \cdot 12H_2O$	Sr H_2O	9.67 23.75	9.67 23.85	Rhombic plates
9	Barium salt $(C_{15}H_9O_5S)_2Ba \cdot 9H_2O$	Ba H_2O	15.25 18.40	15.23 17.97	Poorly developed lamellar crystals
10	Zinc salt $(C_{15}H_9O_5S)_2Zn \cdot 7H_2O$	Zn H_2O	8.16 15.14	8.23 15.88	Lamellar crystals
11	Cadmium salt $(C_{15}H_9O_5S)_2Cd \cdot 4H_2O$	Cd H_2O	14.48 10.12	14.28 9.15	Very fine undeveloped crystals
12	Manganese salt $(C_{15}H_9O_5S)_2Mn \cdot 3H_2O$	Mn H_2O	7.50 7.23	7.21 7.59	Fine prisms
13	Cobalt salt $(C_{15}H_9O_5S)_2Co \cdot 6H_2O$	Co H_2O	7.54 15.12	7.66 14.04	Poorly developed plates
14	Nickel salt $(C_{15}H_9O_5S)_2Ni \cdot 5H_2O$	Ni H_2O	7.77 12.30	7.81 11.99	Poorly developed plates
15	Ammonium salt $C_{15}H_9O_5SNH_4$	N	4.47	4.38	Prismatic crystals
16	Aniline salt $C_{15}H_{10}O_5S \cdot An$	N	3.70	3.54	Long prisms
17	Pyridine salt $C_{15}H_{10}O_5S \cdot Py$	N	3.78	3.67	Short hexahedral crystals
18	Quinoline salt $C_{15}H_{10}O_5S \cdot Ch$	N	3.62	3.25	Prisms

EXPERIMENTAL

2-Phenyl-1,3-indanedione-2-sulfonic acid. To a suspension of 2.2 g of 2-phenyl-1,3-indanedione in 10 ml of 1,2-dichloroethane was added a mixture of 2 ml of acetic anhydride, 0.75 ml of 98% sulfuric acid, and 5 ml of 1,2-dichloroethane. The 2-phenyl-1,3-indanedione dissolved readily. The reaction mixture was cooled with ice, and a white precipitate of the sulfonic acid began to form after approximately 1 hr. After several hours, the precipitate was separated and washed with dry ether. The yield was 2.5 g (77%). The sulfonic acid was readily soluble in water and alcohol and slightly soluble in dry ether. The m.p. was 128 130°. The compound slowly decomposed on standing in air.

Found %: S 10.40. $C_{15}H_{10}O_5S$. Calculated %: S 10.60.

A series of salts of 2-phenyl-1,3-indanedione-2-sulfonic acid (Table 2) was prepared by our previously described method [2,3]. When crystallized from an aqueous alcohol solution, the sodium salt formed the trihydrate, while the anhydrous salt crystallized from aqueous solution.

Sulfonation of 2-phenyl-1,3-indanedione with chlorosulfonic acid. a) In dioxane. To a suspension of 6.66 g of 2-phenyl-1,3-indanedione in 30-35 ml of dry dioxane was added 3.2 ml of chlorosulfonic acid. The 2-phenyl-1,3-indanedione went into solution. The reaction mixture was allowed to stand for 5-6 hr, and the precipitated crystals were then separated, dissolved in water, salted out with sodium chloride, and recrystallized from dilute alcohol. The sodium salt of 2-phenyl-1,3-indanedione-2-sulfonic acid precipitated as yellow prisms (52%).

Sulfonation in diethyl ether was carried out in a similar manner; however, the yield was lower (Table 1).

b) In 1,2-dichloroethane. To a suspension of 6.66 g of 2-phenyl-1,3-indanedione in 30-35 ml of dry 1,2-dichloroethane was added 7 g of chlorosulfonic acid. Hydrogen chloride was evolved, and a resinous, violet-colored precipitate was formed. The flask was loosely stoppered and allowed to stand for 4-5 hr; from time to time, the flask was opened slightly, and the contents were agitated. Water (70-80 ml) was added, and resinous precipitate dissolved, imparting to the aqueous layer a red color. The aqueous layer was separated and saturated with sodium chloride. The resulting voluminous precipitate was separated by filtration and crystallized from alcohol. The sodium salt of 2-phenyl-1,3-indanedione-4'-sulfonic acid was obtained in the form of dark red prisms. The yield was 38%.

Found %: S 9.22. $C_{15}H_9O_5SNa$. Calculated %: S 9.89.

Sulfonation in chloroform, carbon tetrachloride, and isooctane was carried out in a similar manner (Table 1).

Benzylthiuronium salt. Saturated aqueous solutions of benzylthiuronium chloride and the sodium salt of 2-phenyl-1,3-indanedione-4'-sulfonic acid were mixed, and the resulting precipitate of the benzylthiuronium salt was recrystallized from a small amount of alcohol. The salt formed dark red prisms. The m.p. was 192°.

Found %: N 6.04. $C_{23}H_{18}O_5N_2S_2$. Calculated %: N 5.99.

Cleavage of the sodium salt of 2-phenyl-1,3-indanedione-4'-sulfonic acid. A mixture of 1 g of the sodium salt, 1 g of sodium hydroxide, and several drops of water were heated in a hard-glass test tube. The melt was treated with 5-7 ml of water, and concentrated hydrochloric acid was added to the solution until an acid reaction was obtained. The phthalic acid was extracted with ether, and the ether was distilled. The residue gave a positive fluorescein reaction. After extraction of the phthalic acid, the aqueous layer was evaporated to dryness, and the residue was heated to 50° with phosphorus pentachloride. Ice was added to the reaction mixture, and this was followed by the addition of carbon tetrachloride. The mixture was agitated and allowed to settle, and the carbon tetrachloride layer was separated. The carbon tetrachloride was carefully evaporated, and the residue was treated with aniline. The resulting anilide of p-toluenesulfonic acid was purified by crystallization from a mixture of alcohol and diethyl ether. The m.p. was 101-103° [4]. A mixture of this material with a known sample of p-toluenesulfonanilide showed no depression of the melting point.

Sodium salt of 2-bromo-2-phenyl-1,3-indanedione-4'-sulfonic acid. To an aqueous solution of 3.24 g of the sodium salt of 2-phenyl-1,3-indanedione-4'-sulfonic acid in 35-40 ml of water was added a solution of 1.6 g of bromine in 5 ml of glacial acetic acid. The resulting slightly yellowish solution was saturated with sodium chloride. The sodium salt of 2-bromo-2-phenyl-1,3-indanedione-4'-sulfonic acid precipitated. Crystallization from dilute alcohol gave colorless prisms. The yield was 2.6 g (64.5%).

Found %: Br 20.30. $C_{15}H_8O_5SBrNa$. Calculated %: Br 19.82.

Potassium salt. This was prepared similarly to the sodium salt.

Found %: Br 19.48; S 8.31. $C_{15}H_8O_5SBrK$. Calculated %: Br 19.06; S 7.64.

Aniline salt of 2-anilino-2-phenyl-1,3-indanedione-4'-sulfonic acid. The sodium salt of 2-bromo-2-phenyl-1,3-indanedione 4'-sulfonic acid was reacted with excess aniline. There was an exothermic reaction, and the mixture subsequently hardened. The mass was triturated with ether to remove excess aniline and then with water to remove aniline hydrochloride. The residual aniline salt of 2-anilino-2-phenyl-1,3-indanedione-4'-sulfonic acid could be crystallized from water, alcohol, dioxane, or acetone. Crystallization yielded fine, yellowish prisms. The compound melted at 305-307° (with decomposition).

Found %: N 5.91. $C_{27}H_{22}O_5N_2S$. Calculated %: N 5.76.

Preparation of the sodium salt of 2-phenyl-1,3-indanedione-4'-sulfonic acid from benzalphthalide. To 6.66 g of benzalphthalide in 30-35 ml of dry 1,2-dichloroethane was added 3.9 ml of chlorosulfonic acid. A greenish precipitate soon separated from the resulting homogeneous mixture. The mixture was agitated from time to time, and after 3-4 hr it was treated with 80-100 ml of water. The aqueous layer was separated and saturated with sodium chloride. The sodium sulfonate precipitated. Structure (IV) is proposed for this salt. The salt was separated and treated with a mixture of 150 ml of methyl alcohol and sodium methylate, which was prepared from 50 ml of methyl alcohol and 4 g of sodium. The methyl alcohol was almost completely distilled, the residue was extracted with 70-80 ml of water, and hydrochloric acid was added to the aqueous solution until an acid reaction was obtained. The solution was saturated with sodium chloride, and a dark red precipitate of the sodium salt of 2-phenyl-1,3-indanedione-4'-sulfonic acid formed. This was recrystallized from alcohol.

Found %: Na 6.90. $C_{15}H_9O_5SNa$. Calculated %: Na 7.08.

SUMMARY

1. 2-Phenyl-1,3-indanedione-2-sulfonic acid was obtained when 2-phenyl-1,3-indanedione was sulfonated with a mixture of concentrated sulfuric acid and acetic anhydride in nonpolar solvents.

2. 2-Phenyl-1,3-indanedione-4'-sulfonic acid was obtained when 2-phenyl-1,3-indanedione was sulfonated with chlorosulfonic acid in 1,2-dichloroethane, chloroform, carbon tetrachloride, or isooctane. The compound was characterized by means of its benzylthiuronium salt. This same compound was prepared by sulfonation of benzalphthalide and subsequent rearrangement of the sulfonation product by means of sodium methylate.

3. 2-Phenyl-1,3-indanedione-2-sulfonic acid was obtained when 2-phenyl-1,3-indanedione was sulfonated with chlorosulfonic acid in dioxane or in diethyl ether.

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SYNTHESIS OF VINYL MONOMERS

XI. THE REACTION OF VINYLACETYLENE WITH NICKEL CARBONYL: 1-VINYL-3-CYCLOHEXENE-1,4-DICARBOXYLIC ACID AND ITS DERIVATIVES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3972-3978, December, 1960
Original article submitted January 11, 1960

We have previously studied the reaction of certain alkylacetylenes with nickel carbonyl in alcoholic media, and we have established that such reactions yield α alkylacrylates [1] in conformity with Markovnikov's rule.

It would be expected that the interaction of vinylacetylenes with nickel carbonyl in alcoholic media would result in the formation of esters of α-vinylacrylic acid.

$$4CH_2=CH-C\equiv CH + Ni(CO)_4 + 2HCl + 4ROH \rightarrow 4CH_2=CH-\underset{\displaystyle COOR}{\overset{\displaystyle |}{C}}=CH_2 + NiCl_2 + H_2$$

However, under the conditions usually used for these reactions, in place of the esters expected on the basis of the previous work, dimers of these esters were obtained. We were unable to stop the reaction at the monomeric ester stage by carrying the reaction out at lower temperatures or by the use of solvents and the addition of hydroquinone. The reaction products were always esters of a dicarboxylic acid having the composition $C_8H_{10}(COOH)_2$ (under the conditions studied). The formation of esters of vinylacrylic acid dimer could be the result of condensation of two molecules of the normal product of the reaction of vinylacetylene with nickel carbonyl—an ester of vinylacrylic acid. The most probable of such condensations would be condensations leading to a significant number of isomers with four- and six-carbon atom rings. It is likewise not possible to exclude the formation of dihydrodimer by hydrogenation of the vinylacrylic acid ester by hydrogen evolved during the reaction.

Determination of the parachors of these individual dimeric esters and their dihydro and tetrahydro derivatives unequivocally showed that the dimer is a cyclic derivative. Since the values of the parachors calculated for structures with four- and six-membered rings were closely similar and the difference between them was within the limits of experimental error, chemical methods were also used as an aid in the determination of the structure of these dimers.

When the acid $C_8H_{10}(COOH)_2$, obtained by saponification of the dimeric ester, was heated at 270-290°, quantitative decarboxylation to a hydrocarbon—vinylcyclohexene—occurred. Hydrogenation of this hydrocarbon at atmospheric pressure over a palladium catalyst gave vinylcyclohexane. Further hydrogenation of this compound under pressure converted it to ethylcyclohexane. This series of conversions indicates that the dimeric esters formed by the reaction of vinylacetylene with nickel carbonyl are derivatives of vinylcyclohexenedicarboxylic acid.

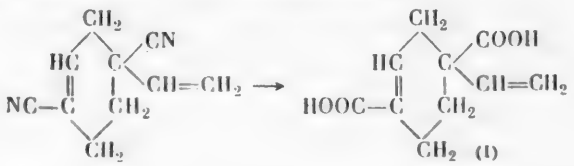
The action of sulfuric acid on vinylcyclohexenedicarboxylic acid gave p-ethylbenzoic acid, which was identified by the constants of the acid itself and those of the ethyl ester and the mononitro derivative; these values were in good agreement with the published values. However, the amide synthesized from the chloride of the

p-ethylbenzoic acid differed sharply in melting point (161°) from p-ethylbenzamide (m.p. 115-116°) synthesized from ethylbenzene, HCN, and HCl in the presence of $AlCl_3$ [2]. Obviously, the literature value is in error and was measured for an isomeric compound. As a matter of fact, oxidation of a sample of our p-ethylbenzoic acid gave terephthalic acid, which was identified in the form of its methyl ester (m.p. 141°) and its chloride (m.p. 40°); this confirms the above statement.

Destructive oxidation of the dimeric acid with the formation of p-ethylbenzoic and terephthalic acids indicated that the substituents (vinyl and carboxyl groups) in the dimeric, cyclohexene acid are located in 1,4-positions with respect to each other. The position of the second carboxyl group in this molecule was still not clear at this point. It could be either in the side chain, i.e., attached to the vinyl group, or it could replace a second hydrogen in the ring at the 4-position with respect to the first carboxyl. In order to clarify this point, the ethyl ester of the vinylcyclohexenedicarboxylic acid was dehydrogenated by heating (at 300°) with selenium and sulfur, and it was also brominated with bromosuccinimide with subsequent elimination of hydrogen bromide by means of quinoline. In neither case was an aromatic derivative formed.

Thus, the interaction of vinylacetylene with nickel carbonyl in alcoholic media takes place with the formation of esters of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid (I).

In a note published prior to the completion of the present investigation [3], the product of the reaction of vinylacetylene with nickel carbonyl and alcohol was erroneously stated to be α-(4-carbethoxycyclohexen-3-yl)-acrylic acid. That this statement is erroneous is confirmed by the fact that the vinylcyclohexenedicarboxylic acid prepared in the present work was identical to vinylcyclohexenedicarboxylic acid prepared by hydrolysis of the product of the Diels-Alder condensation of 2-cyanobutadiene [4].



(I)

The formation of the dihydro derivatives of vinylcyclohexenedicarboxylic acid esters can readily be accomplished by hydrogenation of the esters with the calculated amount of hydrogen at atmospheric pressure over palladium. These dihydro derivatives, like the esters of vinylcyclohexenedicarboxylic acid, are converted by the action of sulfuric acid to p-ethylbenzoic acid. This suggests that the dihydro compounds are derivatives of 1-ethyl-3-cyclohexene-1,4-dicarboxylic acid. Further hydrogenation of these esters of the dihydro acid takes place slowly. It does go almost to completion in the case of the diethyl ester, but does so with difficulty; it takes place even less readily in the case of the dimethyl ester (80-85% hydrogenation); and the dibutyl ester does not hydrogenate at all, under the above conditions. Completely hydrogenated esters of 1-ethylcyclohexene-1,4-dicarboxylic acid can be obtained by carrying out the hydrogenation under pressure at elevated temperatures.

In contrast to esters of the acids described above, esters of ethylcyclohexanedicarboxylic acid undergo saponification by alcoholic alkali at only one ester group, and the acid esters are formed; complete saponification can be obtained by heating (at 200°) with hydrochloric acid in sealed tubes.

Various derivatives (acid esters, chlorides, amides, and others) were prepared during the investigation of the above acids. These derivatives are described in the experimental section.

EXPERIMENTAL

A. Preparation of 1-Vinyl-3-cyclohexene-1,4-carboxylic Acid and Its Derivatives

1. Preparation of the dimethyl ester. A reaction mixture consisting of 26 g of liquid vinylacetylene, 21.3 g of nickel carbonyl, 50 g of methyl alcohol containing 9.1 g of hydrogen chloride, and 35 g of ether was held at 40° for 6 hr. The reaction mixture was then cooled, treated with an aqueous solution of sodium chloride, washed with water, and dried. The ether was evaporated, and the mixture was twice distilled under vacuum. There was obtained 20.1 g of the dimethyl ester of 1-vinyl-3-cyclohexene-1,4 dicarboxylic acid.

B.p. 120-121° (1 mm), $n^{20}D$ 1.4901, d^{20}_4 1.1222, MR_D 57.72; calc. 57.60.

Found %: C 63.63, 63.74; H 7.45, 7.53. $C_{12}H_{16}O_4$. Calculated %: C 64.28; H 7.14.

2. Preparation of the diethyl ester. a) From vinylacetylene, nickel carbonyl, and ethyl alcohol. The reaction was carried out in the manner described for Expt. 1. The diethyl ester, isolated by repeated distillation under vacuum, was a colorless liquid possessing an agreeable odor.

B.p. 144.5-145° (3 mm), $n^{20}D$ 1.4782, d^{20}_4 1.0637, MR_D 67.08; calc. 66.79.

Found %: C 65.85, 65.98; H 7.97, 8.06. $C_{14}H_{20}O_4$. Calculated %: C 66.66; H 7.94.

b) From the chloride of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid. A mixture of 17.7 g of the chloride with an b.p. of 140-141° (5 mm), $n^{20}D$ 1.5360, (see below for preparation) and 7.7 g of anhydrous alcohol was heated at 80-85° until the evolution of hydrogen chloride ceased. There was obtained 15.5 g of the ester.

B.p. 143.5° (5 mm), $n^{20}D$ 1.4812, d^{20}_4 1.0647, MR_D 67.38.

Found %: C 65.35, 65.27; H 7.94, 8.23.

The diethyl ester prepared from the acid chloride was a purer preparation than the ester prepared by method "a," since it was difficult to free the latter compound completely of traces of its associated impurities.

3. Preparation of the di n-butyl ester. a) From vinylacetylene, nickel carbonyl, and n-butyl alcohol. The reaction was carried out under conditions similar to those described for Expt. 1. In contrast to Expts. 1 and 2, the reaction proceeded more sluggishly and was accompanied by the formation of a significant amount of tar. The dibutyl ester was separated by distillation. It was a colorless liquid, and was obtained in 12% yield.

B.p. 182-184° (5 mm), $n^{20}D$ 1.4757, d^{20}_4 1.0135.

Found %: C 68.80, 68.95; H 9.17, 9.16. $C_{18}H_{28}O_4$. Calculated %: C 70.13; H 9.09.

b) From the chloride of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid. A mixture of 33.7 g of the acid chloride and 33 g of anhydrous n-butyl alcohol was heated on a boiling water bath for about 2 hr. Distillation of the reaction products yielded 40.2 g of pure dibutyl ester.

B.p. 172° (1.5 mm), $n^{20}D$ 1.4757, d^{20}_4 1.0158, MR_D 85.47; calc. 85.26.

Found %: C 70.05, 69.62; H 10.51, 10.54. $C_{18}H_{28}O_4$. Calculated %: C 70.13; H 9.09.

4. Preparation and conversions of acid (I). a) Preparation of the acid. A mixture of 35.9 g of the diethyl ester (b.p. 140° at 3 mm) and 17.4 g of KOH dissolved in 160 ml of alcohol was refluxed for 2 hr. The reaction mixture was cooled, and the potassium salt, which precipitated as a white powder, was separated and dissolved in water. The aqueous solution of the salt was made acid with hydrochloric acid, and a white precipitate formed. The product was recrystallized, and 22.3 g of a substance with an m.p. of 233-234° (from 40% CH_3COOH) was obtained in the form of needles with a square cross section. An additional 2.5 g of the acid was obtained from the mother liquor. The over-all yield was 88.5%. The pure acid, obtained by a second recrystallization, melted at 235-236° (with decomposition).

Found %: C 61.11, 60.70; H 6.08, 6.27; H_{act} 1.00, 0.99. $C_{10}H_{12}O_4$. Calculated %: C 61.22; H 6.12; H_{act} 1.03.

b) Thermal decarboxylation of the acid – preparation of vinyl cyclohexane and ethylcyclohexane. A sample of 42 g of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid (m.p. 234-235°) was heated at 270-290°. There was considerable evolution of gas and distillation of decomposition products. The liquid condensate amounted to 11.8 g. Distillation of this material yielded 10.4 g of vinylcyclohexene with a b.p. of 138-139°, $n^{20}D$ 1.483, d^{20}_4 0.8452.

This compound was hydrogenated in the presence of palladous chloride at room temperature and atmospheric pressure. From 10.2 g of hydrogenation products was isolated 5.0 g of vinylcyclohexane.

B.p. 132.5-133°, $n^{20}D$ 1.4531, d^{20}_4 0.8156.

Literature values [5]: b.p. 131° (749 mm), $n^{20}D$ 1.450, d^{20}_4 0.8166.

The vinylcyclohexane was subjected to further hydrogenation in the presence of $PdCl_2$ at atmospheric pressure. This gave ethylcyclohexane.

B.p. 129.5-130.5° (741 mm), $n^{20}D$ 1.4327, d^{20}_4 0.7880, MR_D 36.92; calc. 36.94.

Literature values [6]: b.p. 130-131°, $n^{20}D$ 1.4323, d^{20}_4 0.784.

c) The action of sulfuric acid; conversion to p-ethylbenzoic acid. A sample of 3 g of acid (I) was heated with 25 ml of concentrated sulfuric acid at 100-130° until evolution of gas ceased. The reaction mixture was cooled and poured into ice water. The resulting precipitate (2.4 g) was separated and steam distilled. From the distillate was obtained 1 g of p-ethylbenzoic acid crystals. The square prisms melted at 112-113°. The acid was also identified as its ethyl ester, b.p. 127° (13 mm), $n^{20}D$ 1.5050, d^{20}_4 1.0110 [8]. It was further identified by preparation of the nitro derivative with an m.p. of 156° [7] and by oxidation to terephthalic acid.

The amide was prepared by passing ammonia into 0.1 g of the acid chloride in 1.5 ml of ether. It was obtained in the form of colorless lamellar crystals with an m.p. of 161-162° (from water).

Found %: N 9.42, 9.63. $C_9H_{11}ON$. Calculated %: N 9.49.

5. Preparation of the dichloride. A mixture of 20 g of acid (I) and 45 g of phosphorus pentachloride was heated at 80-85° until the evolution of hydrogen chloride had ceased. The mixture was then distilled under vacuum. The acid chloride was a liquid with a very slight yellowish green color; b.p. 140-141° (5 mm), $n^{20}D$ 1.5360, d^{20}_4 1.2916. Hydrolysis with water reconverted the acid chloride to the dienic dicarboxylic acid. A mixture of this acid with a sample of the original acid showed no depression of the melting point.

Found %: C 51.98, 51.88; H 4.62, 4.56; Cl 30.50, 30.44. $C_{16}H_{20}O_2Cl_2$. Calculated %: C 51.50; H 4.29; Cl 30.47.

The diamide of 1-vinyl 3-cyclohexene-1,4-dicarboxylic acid was prepared by treatment of an ether solution of the dichloride with ammonia. The crystals melted at 187°.

B. Preparation of 1-Ethyl-3-cyclohexene-1,4-dicarboxylic Acid and Its Derivatives

6. Preparation of the dimethyl ester. A solution of 50 g of the dimethyl ester of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid (b.p. 143-145° at 4 mm) in 150 ml of alcohol containing 0.33 g of $PdCl_2$ was hydrogenated at room temperature and atmospheric pressure. The hydrogenation was continued until 5.8 liters of hydrogen (1 mole of H_2 per mole of ester) had been absorbed. The hydrogenation product was distilled under vacuum to isolate the dimethyl ester of 1 ethyl-3-cyclohexene-1,4-dicarboxylic acid.

B.p. 141-142° (4 mm), $n^{20}D$ 1.4793, d^{20}_4 1.1016, MR_D 58.11; calc. 58.02.

Found %: C 64.26, 64.44; H 8.26, 8.25. $C_{12}H_8O_4$. Calculated %: C 63.71; H 7.96.

7. Preparation of the diethyl ester. a) By hydrogenation of the diethyl ester of acid (I). The hydrogenation was carried out under the conditions described for Expt. 6. The ester – a colorless liquid – was isolated by two distillations.

B.p. 146.5° (4 mm), $n^{20}D$ 1.4687, d^{20}_4 1 0488, MR_D 67.53; calc. 67.26.

Found %: C 66.75, 66.44; H 8.96, 8.86. $C_{14}H_{22}O_4$. Calculated %: C 66.14; H 8.66.

b) From the chloride of 1-ethyl-3-cyclohexene-1,4-dicarboxylic acid. A mixture of 5.3 g of the acid chloride (b.p. 147-148° at 3 mm) (prepared as described below) and 3.5 g of anhydrous alcohol was heated on a boiling water bath for 2 hr. Two distillations yielded 4.7 g of the diethyl ester.

B.p. 149.5° (4 mm), $n^{20}D$ 1.4712, d^{20}_4 1.0507, MR_D 67.59.

Found %: C 65.82, 66.11; H 9.21, 9.25.

8. Preparation of 1-ethyl-3-cyclohexene-1,4-dicarboxylic acid. A mixture of 35 g of the dimethyl ester (b.p. 144-144.5° at 5 mm) and 23 g of KOH dissolved in 115 ml of alcohol was refluxed for 5 hr. The salt, which precipitated when the reaction mixture was cooled, was dissolved in 200 ml of water. Upon acidification of the solution with 25 ml of hydrochloric acid a white precipitate formed; m.p. 220-228°. Recrystallization yielded 18.5 g of 1-ethyl-3-cyclohexene-1,4-dicarboxylic acid in the form of lustrous prisms with an m.p. of 233-234° (from aqueous methanol).

Found %: C 60.38, 60.34; H 7.10, 7.47. $C_{10}H_{14}O_4$. Calculated %: C 60.60; H 7.07.

p-Ethylbenzoic acid was prepared by the action of sulfuric acid on this acid under conditions analogous to those described for Expt. 4.

9. Preparation of the dichloride. A mixture of 5 g of the acid (m.p. 234°) and 12 g of phosphorus pentachloride was heated for 1.5 hr on a boiling water bath. After removal of the phosphoryl chloride and distillation of the product under vacuum, there was obtained 3.6 g of the dichloride.

B.p. 144-145° (2 mm), $n^{20}D$ 1.5220, d^{20}_4 1.2651.

Found %: Cl 30.20, 29.88. $C_{10}H_{12}O_2Cl_2$. Calculated %: Cl 30.16.

Treatment of an ether solution of the chloride with gaseous ammonia gave the amide of 1-ethyl-3-cyclohexene-1,4-dicarboxylic acid. The crystals melted at 204°.

C. Preparation of 1-Ethylcyclohexane-1,4-dicarboxylic Acid and Its Derivatives

10. Preparation of the dimethyl ester. A solution of 15.6 g of the dimethyl ester of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid in 100 ml of alcohol containing 0.1 g of palladous chloride was hydrogenated, first at room temperature and atmospheric pressure, and then at 70-80° and a pressure of 35 atm. Distillation of the reaction product yielded the dimethyl ester of 1-ethylcyclohexane-1,4-dicarboxylic acid.

B.p. 109-110° (3 mm), $n^{20}D$ 1.4580, d^{20}_4 1.0697, MR_D 58.15; calc. 58.99.

Found %: C 63.09, 63.28; H 8.71, 8.68. $C_{12}H_{20}O_4$. Calculated %: C 63.16; H 8.77.

11. Preparation of the diethyl ester. A solution of 12.4 g of the diethyl ester of vinylcyclohexenedicarboxylic acid in 68 ml of alcohol containing 0.08 g of $PdCl_2$ was hydrogenated under the conditions described for the preparation of the dimethyl ester. The diethyl ester was separated by vacuum distillation.

B.p. 125° (0.5 mm), $n^{20}D$ 1.4514, d^{20}_4 1.0207, MR_D 67.63; calc. 67.72.

Found %: C 64.74, 66.63; H 9.92, 9.95. $C_{14}H_{24}O_4$. Calculated %: C 65.62; H 9.38.

12. Preparation of the di-n-dibutyl ester. The preparation of this ester was carried out in a manner similar to that described for the preparation of the diethyl and dimethyl esters. The ester, after two distillations, was a colorless liquid with a weak ester-like odor.

B.p. 165.6-166.5° (1 mm), $n^{20}D$ 1.4542, d^{20}_4 0.9853, MR_D 85.16; calc. 85.19.

Found %: C 68.70, 68.97; H 10.73, 10.32. $C_{18}H_{32}O_4$. Calculated %: C 69.23; H 10.25.

13. Preparation of the monomethyl ester. A mixture of 3 g of the dimethyl ester of 1-ethylcyclohexane-1,4-dicarboxylic acid (b.p. 109-110° at 3 mm) and 8 g of concentrated hydrochloric acid was allowed to stand at room temperature for 18 hr. The precipitated crystals, 2.1 g, were recrystallized from water; the square prisms melted at 112-114°, and were readily soluble in acetone, ethyl acetate, and ethyl and methyl alcohols.

Found %: C 61.08, 61.94; H 8.62, 9.44; H_{act} 0.472, 0.460. $C_{11}H_{18}O_4$. Calculated %: C 61.68; H 8.41; H_{act} 0.470.

14. Preparation of the monoethyl ester. A mixture of 5 g of the diethyl ester of 1-ethylcyclohexane-1,4-dicarboxylic acid (b.p. 127° at 1 mm) and 2.2 g of KOH dissolved in 15 ml of alcohol was refluxed for 2 hr. The solvent was evaporated under vacuum, and the residue (the potassium salt) was dissolved in water. The aqueous solution was made acid with hydrochloric acid. The oil which separated from the acid solution was extracted with ether, and the ether solution was distilled under vacuum. There was obtained 1.8 g of a fraction with a b.p. of 178-181° (2 mm) and an m.p. of 56-61°. After being twice recrystallized from ligroin, the small cubes melted at 61-62°.

Found %: C 63.22, 63.17; H 9.23; H_{act} 0.428, 0.428. $C_{12}H_{20}O_4$. Calculated %: C 63.16; H 8.77; H_{act}. 0.442.

15. Preparation of 1-ethylcyclohexanedicarboxylic acid. A mixture of 10 g of the diethyl ester of ethylcyclohexanedicarboxylic acid and 20 g of concentrated hydrochloric acid was heated in a sealed tube at 200° for

5 hr. When the mixture was cooled, crystals (7.7 g) with an m.p. of 148-151° separated. Two recrystallizations of the material from water yielded square prisms with an m.p. of 156-157°. These crystals were soluble in methyl and ethyl alcohols, acetone, ether, and acetic acid, and were insoluble in chloroform.

Found %: C 60.07, 59.92; H 8.87, 8.84; H_{act} 1.078, 1.019. $C_{10}H_{16}O_4$. Calculated %: C 60.00; H 8.00; H_{act} 1.007.

16. Preparation of the dichloride. A mixture of 4 g of the acid (m.p. 155-156°) and 10.5 g of phosphorus pentachloride was heated for 2 hr on a boiling water bath. The reaction product was distilled, and 3.6 g of the dichloride was obtained. The dichloride had a b.p. of 132-132.5° (3 mm), $n^{20}D$ 1.4972.

Found %: C 51.61, 51.73; H 6.31, 6.29; Cl 30.3, 30.2. $C_{10}H_{14}O_2Cl_2$. Calculated %: C 50.63; H 5.90; Cl 29.9.

SUMMARY

1. The interaction of vinylacetylene with nickel carbonyl and alcohols was investigated. The reaction yields esters of 1-vinyl-3-cyclohexene-1,4-dicarboxylic acid.

2. Catalytic hydrogenation of these esters over palladium resulted in the formation of products of the addition of two and of four atoms of hydrogen to the ester. The first products were derivatives of 1-ethyl-3-cyclohexene-1,4-dicarboxylic acid (or the isomeric 1-vinylcyclohexane-1,4-dicarboxylic acid). The second products were derivatives of 1-ethylcyclohexane-1,4-dicarboxylic acid.

3. The preparation and properties of various derivatives (esters, acids, acid chlorides, amides, etc.) of the above acids are described.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

REACTION OF ALDEHYDES WITH TRIALKYL PHOSPHITES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3979-3987, December, 1960
Original article submitted July 31, 1959

A number of papers have been devoted to the reaction of aldehydes with trialkyl phosphites, in which it was indicated that aliphatic and aromatic aldehydes form esters of (1-alkoxyalkyl)phosphonic acids [1], whereas the α,β-unsaturated aldehydes give 1,4-addition products [2, 3]; the esters of phenylphosphonous acid react in a similar manner [4].

$$RCH{=}O + (C_2H_5O)_3P \longrightarrow (C_2H_5O)_2P(O)CH(R)OC_2H_5 \quad (1)$$

$$CH_2{=}CH{-}CH{=}O + (C_2H_5O)_3P \longrightarrow (C_2H_5O)_2P(O)CH_2{-}CH{=}CHOC_2H_5 \quad (2)$$

In the enumerated papers the decision as to the structure of the obtained compounds was based mainly on the phosphorus analysis and the molecular refraction values. Only for the reaction product of trialkyl phosphite and acrolein was it shown that the hydrolysis of this compound leads to the formation of phosphonopropionaldehyde. On the assumption that these data are not sufficient to prove the described transformations, we deemed it expedient to return to their study.

Starting with triethyl, tripropyl and tributyl phosphites and several aldehydes, including both unsaturated and aromatic aldehydes, we prepared a number of phosphorus-containing derivatives, the constants and analysis data for which are given in the table.

The analysis data and the molecular weights of the obtained products indicate that only the reaction products of the phosphites with aromatic aldehydes (benzaldehyde, but not salicylaldehyde) have a structure corresponding to scheme (1); the composition of the reaction product of phosphite and acrolein corresponds to scheme 2. A different situation exists in the case of the reaction products of trialkyl phosphites and aliphatic aldehydes, the composition of which, especially the amount of alkoxy groups, differs materially from that calculated in accordance with scheme 1. At the same time, the method used to determine the alkoxy groups in the case of compounds Nos. 5 and 8 (table) and also the specially synthesized diethyl ester of methoxymethylphosphonic acid (No. 7, table) proved to be satisfactory.

The structure of the reaction products of trialkyl phosphites and aliphatic aldehydes was studied on the example of butyraldehyde. It proved that the same (1-hydroxybutyl)phosphonic acid (m.p. 162°) was formed in all cases when compounds Nos. 2, 3 and 4 were hydrolyzed with hydrochloric acid. In addition to the indicated acid, some unidentified tarry substances are formed in the hydrolysis. However, if the hydrolysis is run under mild conditions, comparable to those used for hydrolysis of acetals [6], it becomes possible to isolate butyraldehyde in 70% yield. The other product that is formed here proved to be the corresponding ester of (1-hydroxybutyl)phosphonic acid. The infrared spectrum of compounds Nos. 2, 3 and 4 does not show absorption in the region of the C = C and C = O bonds (5.5-6.5 μ). All of this information makes it possible to assign the following structure to the indicated compounds and to depict the hydrolysis scheme as follows:

Expt. No.	Reaction components	Boiling point (pressure in mm)	Found							Calculated									
										R'CH(OR)PO(OR)$_2$					R'CH[OCHR'(OR)]PO(OR)$_2$				
			n_D^{20}	d_{20}	M	% C	% H	% P	OR	M	% C	% H	% P	OR	M	% C	% H	% P	OR
1	$(C_2H_5O)_3P + CH_3CHO$	142°(5)	1.4260	1.110	246.5	47.42, 47.26	8.82, 8.60	11.28, 11.29	49.80, 49.84	210	45.6	9.05	14.75	64.3	254	47.25	9.08	12.2	53.25
2	$(C_2H_5O)_3P + CH_3CH_2CH_2CHO$*	140 (1)	1.4385	0.985	305	54.07, 54.00	9.95, 9.56	10.38, 11.44	41.98, 41.40	238	50.5	9.6	13.0	55.8	310	54.4	10.0	10.0	43.5
3	$(C_2H_5O)_3P + CH_3CH_2CH_2CHO$	145 (1)	1.4400	0.943	360	58.20, 58.30	10.66, 10.90	9.58, 9.53	48.66, 48.88	280	54.0	10.35	11.1	63.5	352	58.0	10.5	8.80	50.3
4	$(C_2H_5O)_3P + CH_3CH_2CH_2CHO$	160 (2)	1.4425	0.933	384	62.60, 62.33	10.43, 10.86	8.02, 8.11	54.71, 54.27	322	59.75	10.85	9.64	68.25	394	61.4	10.9	7.9	55.6
5	$(C_2H_5O)_3P + C_6H_5CHO$	179 (1)	1.4915	1.063	267	58.35, 57.98	7.47, 7.70	14.29, 14.00	49.48, 49.16	272	57.5	7.85	14.87	49.6	378	63.75	7.18	8.2	35.7
6	$(C_2H_5O)_3P + HOC_6H_4CHO$	190—193 (3)	1.5010	1.230	271	—	—	—	32.33, 32.05	288	—	—	—	47	410	—	—	—	33.0
7	$(C_2H_5O)_3P + ClCH_2OCH_3$	120 (20)	1.4230	1.088	183	38.93, 39.27	8.42, 8.59	16.86, 16.76	2.85,** 2.80	182	39.6	8.25	17.0	3.0**	—	—	—	—	—
8	$(C_2H_5O)_3P + CH_2=CHCHO$	138—140 (4)	1.4455	1.060	217	47.29, 47.59	8.73, 8.43	13.61, 13.65	57.07, 57.42	—	—	—	—	—	—	—	—	—	—

*When the reaction mixture is subjected to gross distillation it also becomes possible to isolate lower boiling fractions with b.p. 120-135° (1 mm), $n^{20}D$ 1.4340-1.4370, d^{20}_{20} 1.020-1.030, and having a low molecular weight. From their constants these fractions most closely resemble the substance described by Abramov (b.p. 119-120° at 2 mm, $n^{20}D$ 1.4420, d^{20}_4 1.054). Analysis of the indicated fractions gave in %: C 48-51; P 11-13; OC_2H_5 36-39, which apparently corresponds to a mixture containing $CH_3CH_2CH_2CH(OH)PO(OC_2H_5)_2$. The infrared spectrum of the investigated fractions shows an intense absorption band at 5.85 μ, corresponding to the C = O bond, and a band at 2.9-2.95 μ, corresponding to the presence of OH group. The diethyl ester of (1-hydroxybutyl)phosphonic acid, prepared by us specially by the Abramov method [5] from butyraldehyde and diethyl phosphite had b.p. 121° (2 mm), $n^{20}D$ 1.4360, d^{20}_{20} 1.067; found %: C 45.50; H 9.06; P 15.65; OC_2H_5 42.5. M 207.5. Calculated %: C 45.6; H 9.06; P 14.8; OC_2H_5 42.9. M 210. Purer samples of compound No. 2 are obtained if butyraldehyde is reacted with triethyl phosphite that had been previously distilled from sodium, with the reactants taken in the ratio of 1 mole of aldehyde and 2 moles of phosphite.

**Because of the common presence of both methoxyl and ethoxyl groups in the compound, the separate determination of which is difficult, we determined the total amount of alkoxy groups.

$$CH_3CH_2CH_2CH[OCH(OR)CH_2CH_2CH_3]PO(OR)_2$$

conc. HCl / 1–2% HCl (3)

$$CH_3CH_2CH_2CH(OH)PO(OH)_2 \xleftarrow[HCl]{\text{conc.}} CH_3CH_2CH_2CH(OH)PO(OR)_2 +$$
$$+ CH_3CH_2CH_2CHO + ROH$$

If the presented formula is valid, then in the investigated products Nos. 2, 3 and 4 two kinds of alkoxyl groups should be present on the phosphorus and on the carbon. Actually, when the reaction products of butyraldehyde with triethyl and tripropyl phosphites are treated with phosphorus pentachloride they are converted to the dichlorides, which decompose partially on distillation and contain an unsubstituted alkoxy group. It is interesting to mention that in the described reaction a third chlorine atom enters the molecule of the starting compound. This chlorine atom cannot be detected by hydrolysis with water, and it may be assumed that it is found on the carbon attached to the phosphorus, the ease of chlorination of which we had mentioned earlier [7]. Refluxing the acid chloride with hydrochloric acid results in cleavage of the organophosphorus bond and the formation of phosphorous and phosphoric acids, as had been described for the α-ketophosphonic acid [8], apparently formed as an intermediate product in our case.

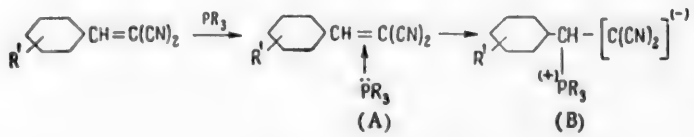
$$CH_3CH_2CH_2CCl[OCH(OR)CH_2CH_2CH_3]POCl_2 \xrightarrow{HCl} [CH_3CH_2CH_2CCl(OH)PO(OH)_2 \rightarrow$$
$$\rightarrow CH_3CH_2CH_2COPO(OH)_2] \rightarrow HPO(OH)_2 + CH_3CH_2CH_2COOH \quad (4)$$

Together with the described products, when trialkyl phosphites are reacted with aldehydes, with the latter taken in excess (1 mole of phosphite per 2 moles of aldehyde), a certain amount of a higher boiling phosphorus-containing product is obtained, the composition of which corresponds to the addition of three moles of aldehydes to the trialkyl phosphite, $(RO)_3P \cdot 3R'CHO$. Hydrolysis of this substance gives butyraldehyde and phosphoric acid, and also a small amount of fractions with b.p. 40-50° and 75-80°, devoid of phosphorus. These two fractions give derivatives – the hydrazones and semicarbazones, corresponding to butyraldol and two carbonyl compounds $C_8H_{16}O$, the structure of which was not investigated. The formation of these substances indicates that under the influence of phosphites the aldehydes undergo various condensation processes, the rates of which are so great that for aliphatic aldehydes, even with an excess of phosphite present (3 moles per mole of aldehyde), it becomes impossible to isolate the adduct of composition $R'CH(OR)PO(OR)_2$.

The investigated reaction of addition of neutral phosphites to aldehydes is a particular case of a larger group of reactions, in which trivalent phosphorus compounds play the role of "ansolvo bases." A detailed survey of these transformations is given in [10] on the examples of trialkyl- or triarylphosphines. The specificity of the phosphites consists in the instability of their "phosphonium" derivatives (stage B), which exhibit a tendency to eliminate the alkyl radical, migrating as cations to the place of the greatest electron density of the reaction complex (stage C).

$$R'CH{=}O + P(OR)_3 \longrightarrow \Big[R'CH{=}O \rightarrow R'CH{-}\overset{(-)}{O} \rightarrow R'CH{-}\overset{(-)}{O} \Big] \rightarrow$$
$$\rightarrow R'CH(OR)PO(OR)_2 \qquad \text{(A)} \qquad \text{(B)} \qquad \text{(C)} \quad (5)$$

The primary addition product (A) may be regarded as being a π-complex, formed by insertion of the phosphorus atom, having an unshared electron pair, at the π-bond of the C=O group. In the case of certain reactions of phosphines, the formed π-complex is stabilized to the comparatively stable bipolar ion, for example, as described in [10].



In the reaction of trialkyl phosphites with carbonyl compounds the formation of the π- complex should facilitate the introduction of negative substituents into the molecule of the latter compounds. Stabilization of the reaction complex in such case is possible along two directions. In accordance with the above described scheme (5) for the formation of α-alkoxyphosphonic esters, the primary addition product is apparently capable at stage (A) or (B), in the presence of other electrophilic compounds, of reactions of the anionotropic telomerization type. In our case this process leads to obtaining addition products composed of 1 mole of phosphite and 2 moles of aldehyde.

$$\left[\underset{\underset{(B)}{\overset{|}{(+)}P(OR)_3}}{R'CH(O^{(-)})-} + R'CH{=}O \longrightarrow \underset{\overset{|}{(+)}P(OR)_3}{R'CH(O-CHR'-O^{(-)})-}\right] \longrightarrow \underset{\overset{|}{PO(OR)_2}}{R'CH(OCHR'(OR)-} \quad (7)$$

The second possible direction of reaction is accomplished by the Perkov rearrangement with formation of the C-O-P linkage.

$$\underset{\underset{(A)}{\overset{\uparrow}{P(OR)_3}}}{R'CH{=}O} \longrightarrow \underset{(D)}{[R'CH]^{(-)}-O-P^{(+)}(OR)_3} \quad (8)$$

Here for halogenated carbonyl compounds a stabilization of the intermediate stage (D) occurs via cleavage of the halogen atom, which is facilitated by the presence of the cationized alkyl of the phosphonium group.

$$\underset{(D)}{[CCl_3CH]^{(-)}-OP^{(+)}(OR)_3} \rightarrow [\underset{Cl^{(-)}}{CCl_2{=}CH-OP^{(+)}(OR)_3}] \longrightarrow$$
$$\longrightarrow CCl_2-CH-OPO(OR)_2 + RCl \quad (9)$$

The formation of complex products in the discussed reaction of phosphites with aldehydes, including the addition products of 1 mole of phosphite and 3 moles of aldehyde, which on hydrolysis give aldehyde and phosphoric acid, is apparently the consequence of the second direction of the process, for example, in accordance with the scheme:

$$\underset{\underset{P(OR)_3}{\overset{\uparrow}{}}}{R'CH{=}O} \longrightarrow \left[[R'CH]^{(-)}-OP^{(+)}(OR)_3 + R'CH{=}O \longrightarrow \underset{\overset{|}{O^{(-)}}}{R'CH-CH(R')OP^{(+)}(OR)_3} \xrightarrow{R'CHO}\right.$$
$$\left. \longrightarrow \underset{\overset{|}{O^{(-)}}}{R'CH-OCHR'-CH(R')OP^{(+)}(OR)_3}\right] \longrightarrow R'CH(OR)OCH(R')CH(R')OPO(OR)_2 \quad (10)$$

EXPERIMENTAL

1. Reaction of triethyl phosphite with acetaldehyde. A mixture of 2.8 g of freshly distilled acetaldehyde and 10.5 g of triethyl phosphite, distilled from sodium, was heated in a sealed ampul at 140-150° for 6 hr. By repeated fractional distillation we were able to isolate 1.8 g of a colorless viscous liquid.

B.p. 142° (5 mm), d^{20}_{20} 1.110, $n^{20}D$ 1.4260.

Found %: C 47.42, 47.26; H 8.82, 8.60; P 11.28, 11.69; OC_2H_5 49.80, 49.84. M 246.5. $C_{10}H_{23}O_5P$. Calculated %: C 47.25; H 9.08; P 12.2; OC_2H_5 53.25. M 254.

2. Reaction of Triethyl Phosphite with Butyraldehyde

a) Using 1 mole of phosphite per mole of aldehyde. The same as before, a mixture of 17.0 g of triethyl phosphite and 7.75 g of butyraldehyde was heated in a sealed ampul. Two fractions were isolated on repeated fractional distillation: 1st, b.p. 117-123° (2 mm), d^{20}_{20} 1.023, $n^{20}D$ 1.4345 (2.6 g), and 2nd, b.p. 140° (1 mm), d^{20}_{20} 0.990, $n^{20}D$ 1.4385 (2.5 g).

The residue in the distillation flask was a viscous liquid (3 g), from which a substance with b.p. 145-155° (1 mm) and higher was isolated.

Analysis of the 1st fraction gave the following results:

Found %: C 46.86, 47.22; H 8.48, 8.00; P 12.84, 12.61; OC_2H_5 37.10, 37.38. M 223. $C_8H_{19}O_4P$. Calculated %: C 45.6; H 9.06; P 14.8; OC_2H_5 42.8. M 210.

Infrared spectrum: strong absorption bands at 2.90-2.95 μ (OH group) and at 8.0-8.15 μ (P = O groups).*

A mixture of 3 g of this fraction and 20 ml of hydrochloric acid was heated under reflux for 3 hr. Evaporation of the mixture in vacuo gave us 1.7 g of crystals with m.p. 162° (from a mixture of acetic acid and acetone).

Found %: C 31.47, 31.58; H 6.82, 7.04; P 19.56, 19.86. Equiv. 158.0, 159.5 (using Methyl orange); 78.4, 78.55 (using phenolphthalein). $C_4H_{11}O_4P$. Calculated %: C 31.2; H 7.15; P 20.00. M 154.

One gram of the obtained acid in alcohol was treated with aniline. After recrystallization from alcohol, m.p. 147° (decomp.).

Found %: C 48.21, 48.35; H 6.55, 6.85; N 5.43, 5.46; P 12.69, 12.41. $C_{10}H_{18}O_4NP$. Calculated %: C 48.5; H 7.3; N 5.67; P 12.6.

As a result, the investigated fraction is impure diethyl ester of (1-hydroxybutyl)phosphonic acid. The melting point of authentic (1-hydroxybutyl)phosphonic acid, obtained by the hydrolysis of the addition product of diethyl phosphite [5] to butyraldehyde, is 162°. The mixed melting point was not depressed.

For the 2nd fraction (b.p. 140° at 1 mm) the found values for the amount of C, H, P, and OC_2H_5 show good agreement with those calculated for the formula $C_{14}H_{31}O_5P$.

The infrared spectrum does not have absorption bands in the region of the valence vibrations of the OH group and the C = C and C = O bonds. A strong absorption band is found at 8.0-8.15 μ (P = O group). Three grams of this fraction was hydrolyzed with 20 ml of hydrochloric acid, as described above. After extraction of the water-insoluble brown tar with ether, the hydrochloric acid solution was evaporated. Here we obtained 1.3 g of an acid with m.p. 162° (from acetic acid), which failed to depress the melting point when mixed with a sample of authentic (1-hydroxybutyl)phosphonic acid. The analysis data for the acid and its aniline salt coincide with those given above.

b) Using 1 mole of triethyl phosphite per 2 moles of butyraldehyde. Repeated fractional distillation of the products obtained from the reaction (carried out under the above described conditions) of 20 g of triethyl phosphite and 18 g of butyraldehyde gave the following fractions: 1st, b.p. 120-125° (2 mm), 2.5 g, d^{20}_{20} 1.030, $n^{20}D$ 1.4350; 2nd, b.p. 140-142° (2 mm), 6.5 g, d^{20}_{20} 0.9853, $n^{20}D$ 1.4385; 3rd, b.p. 150-153° (1 mm), 3.5 g, d^{20}_{20} 1.010, $n^{20}D$ 1.4455.

The 1st fraction analyzes, in %: C 48.78, 48.45; H 9.61, 9.86; P 12.29, 12.70; OC_2H_5 43.34. M 227. Hydrolysis of the fraction yields an acid with m.p. 160-162°. The substance was identified as impure diethyl ester of (1-hydroxybutyl)phosphonic acid (see Expt. 2a).

The 2nd fraction analyzes, in %: C 54.34, 54.39; H 9.73, 9.60; P 10.68, 10.42; OC_2H_5 42.90, 42.63. M 310.

As a result, based on the analysis data and the constants, the substance is identical with the corresponding product obtained in Expt. 2a.

Hydrolysis of the 2nd fraction under mild conditions. Five grams of the substance in 30 ml of 50% aqueous dioxane solution, containing 2% hydrochloric acid, was heated for 30 min, after which the solution was extracted with 150 ml of ether and the ether extract was dried over magnesium sulfate. Half of the extract was treated with 2,4-dinitrophenylhydrazine solution until no more hydrazone precipitated. The total yield of the hydrazone was 1.4 g, including that obtained from the evaporation of the ether.

B.p. 121-122° (from aqueous alcohol).

Found %: C 47.62, 47.73; H 4.75, 4.41; N 21.9, 22.12. $C_{10}H_{12}O_4N_4$. Calculated %: C 47.75; H 4.75; N 22.2.

*The infrared spectra of this and the other compounds described here were graciously run by S. S. Dubov, for which, and also for the joint discussion of the obtained data, we wish to express our sincere thanks.

The mixed melting point with authentic butyraldehyde hydrazone was not depressed. The yield of the hydrazone was about 70%. After distilling off the solvent, the second half of the ether extract was fractionated. Here we obtained about 1.35 g of a fraction with b.p. 120-123° (2 mm), d^{20}_{20} 1.027, and $n^{20}D$ 1.4345, in its constants corresponding to the diethyl ester of (1-hydroxybutyl)phosphonic acid. The yield of the ester was 80%. The aqueous layer of the hydrolyzate was evaporated in vacuo to remove the water and here we obtained 0.2 g of (1-hydroxybutyl)phosphonic acid with m.p. 159-160°.

Treatment of the 2nd fraction with phosphorus pentachloride. Eight grams of the 2nd fraction was added gradually to 24 g of phosphorus pentachloride, after which sulfur dioxide was passed into the reaction mixture until all of the precipitate had dissolved. After two fractional distillations we obtained 2.7 g of an acid chloride with b.p. 150-155° (1 mm), which decomposed partially when distilled, and was stored in solid carbon dioxide: d^{20}_{20} 1.256, $n^{20}D$ 1.4665.

Found %: C 35.48, 35.97; H 5.83, 5.76; P 10.23, 10.53; Cl_{total} 33.27, 33.15; $Cl_{hydrolyzable}$ 22 10, 22.55; OC_2H_5 11.25, 11.97. M 293. $C_{10}H_{20}O_3PCl_3$. Calculated %: C 36.8; H 6.15; P 9.5; Cl_{total} 32 8; $Cl_{hydrolyzable}$ 21.8; OC_2H_5 13.8. M 325.5.

Hydrolysis of the acid chloride. A mixture of 2 g of the acid chloride and 15 ml of hydrochloric acid was refluxed for 5 hr. The brown tarry reaction mass was extracted with ether, after which the water layer was evaporated in vacuo. The oily residue, giving a positive test for phosphoric acid (molybdate reagent) and for phosphorous acid (test with mercuric chloride), was treated with 3 g of aniline. Here we obtained 1.3 g of colorless aniline phosphate crystals, which after recrystallization from aqueous alcohol had m.p. 145-147° (decomp.). The substance does not contain chlorine.

Found %: C 50.95, 51.22; H 6.31, 6.51; N 9.94, 9.80; P 10.87, 10.75. $C_{12}H_{17}O_4N_2P$. Calculated %: C 51.1; H 6.0; N 9.85; P 10.9.

Analysis of the 3rd fraction gave the following results:

Found %: C 55.98, 56.23; H 4.87, 5.10; P 8.49, 8.60; OC_2H_5 35.45, 35.47. M 377. $C_{18}H_{39}O_6P$. Calculated %: C 56.5; H 4.72; P 8.15; OC_2H_5 35.4. M 384.

Hydrolysis of the substance by refluxing with hydrochloric acid gave phosphoric acid. Hydrolysis with 2% HCl in 50% aqueous dioxane solution gave butyraldehyde, isolated as the dinitrophenylhydrazone with m.p. 121°. The mixed melting point with the authentic hydrazone was not depressed.

c) Reaction using 3 moles of triethyl phosphite per mole of butyraldehyde. A mixture of 16.6 g of triethyl phosphite and 2.4 g of butyraldehyde was heated in a sealed ampul for 5 hr at 140-150°. The following fractions were isolated on fractional distillation: with b.p. 120-123° (2 mm), 0.1 g, and with b.p. 137-141° (1 mm), 1.7 g, d^{20}_{20} 1.011, $n^{20}D$ 1.4380, and analyzing in %: C 54.31, 54.13; H 9.06, 8 85; OC_2H_5 41.98, 41.70. M 300 This corresponds to the analysis data and constants for the principal reaction product obtained in Expts. 2a and 2b, and having the formula $C_{14}H_{31}O_5P$.

3. Reaction of tripropyl phosphite with butyraldehyde. A mixture of 13.0 g of tripropyl phosphite and 9 g of butyraldehyde was heated in a sealed ampul for 8 hr at 150°. Repeated fractional distillation gave the following fractions: 1st, b.p. 40-50° (5 mm), 0.4 g; 2nd, b.p. 75-80° (5 mm), 1.5 g, d^{20}_{20} 0.975, $n^{20}D$ 1.4450; 3rd, b.p. 144-145° (1 mm), 9.5 g, d^{20}_{20} 0.943, $n^{20}D$ 1.4400; 4th, b.p. 168-170° (1 mm), 2 g, d^{20}_{20} 0.965, $n^{20}D$ 1.4500.

The 1st fraction (0.5 g) was treated with a solution of dinitrophenylhydrazine. Here we obtained 0.85 g of yellow crystals, which by repeated recrystallization from alcohol were separated into 0.3 g of comparatively soluble crystals with m.p. 83° and 0.2 g of difficultly soluble crystals with m.p. 120°; the mixed melting point of the substance with authentic butyraldehyde hydrazone is depressed sharply (m.p. 87-89°). Both products are devoid of phosphorus.

Analysis of crystals with m.p. 83°.

Found %: C 52.27, 52.65; H 5.64, 5.89; N 17.82, 17.62. $C_{14}H_{20}O_7N_4$. Calculated %: C 52.0; H 6.2; N 17.8.

Analysis of crystals with m.p. 121°.

Found %: C 51.95, 52.07; H 5.83, 6.27; N 17.21, 17.26. $C_{14}H_{20}O_7N_4$. Calculated %: C 52.0; H 6.2; N 17.3.

A m.p. of 120.5-121.5° is given for the dinitrophenylhydrazone of 2-ethylhexanal [11].

From 0.5 g of the 2nd fraction we obtained 0.5 g of a semicarbazone. M.p. 147-148° (from alcohol).

Found %: C 49.53, 49.85; H 8.53, 8.64; N 19.64, 19.38. $C_9H_{19}O_3N_3$. Calculated %: C 49.8; H 8.8; N 19.4.

A m.p. of 147° is given for the semicarbazone of butyraldol [9]. The mixed melting point of the above semicarbazone with the semicarbazone of authentic butyraldol (b.p. 86-88° at 6 mm, d^{20}_{20} 0.988, $n^{20}D$ 1.4960) was not depressed.

For the 3rd fraction the found percent content of C, H, P, and OC_3H_7 and the molecular weight show good agreement with the values calculated for $C_{17}H_{37}O_5P$.

Hydrolysis of the 3rd fraction in concd. hydrochloric acid by the above described method gave 1.1 g of (1-hydroxybutyl)phosphonic acid with m.p. 162° (from acetic acid). The results of the elemental analysis of the acid and its aniline salt for C, H and P, and the values of the gram-equivalents, determined by titrating weighed amounts of the acid in the presence of Methyl orange and phenolphthalein as the indicators, correspond to (1-hydroxybutyl)phosphonic acid.

The hydrolysis of 5 g of the 3rd fraction under mild conditions, using 2% hydrochloric acid in 50% aqueous dioxane solution, gave 1.2 g of butyraldehyde dinitrophenylhydrazone (from $\frac{1}{2}$ of the hydrolyzate) with m.p. 121° and 1.5 g of the dipropyl ester of (1-hydroxybutyl)phosphonic acid.

B.p. 150-152° (5 mm), d^{20}_{20} 0.981, $n^{20}D$ 1.4400.

Found %: C 50.42, 50.35; H 9.12, 9.48; P 12.87, 12.78; OC_3H_7 48.35, 48.63. M 229. $C_{10}H_{23}O_4P$. Calculated %: C 50.5; H 9.7; P 13.0; OC_3H_7 49.5. M 238.

Treatment of the 3rd fraction with phosphorus pentachloride. The 3rd fraction (5.5 g) was added in drops to 15 g of PCl_5, and on conclusion of reaction a stream of SO_2 was passed into the mixture until all of the precipitate had dissolved. After two fractional distillations, accompanied by a partial decomposition of the product, we obtained 1.3 g of an acid chloride, which darkened rapidly in the air.

B.p. 155-160° (1 mm), d^{20}_{20} 1.163, $n^{20}D$ 1.4680.

Found %: C 38.61, 38.23; H 6.98, 6.62; P 10.01, 9.83; Cl_{total} 30.04, 31.30; $Cl_{hydrolyzable}$ 20.55; OC_3H_7 18.09, 18.17. M 305.5. $C_{11}H_{22}O_3PCl_3$. Calculated %: C 38.9; H 6.5; P 9.15; Cl_{total} 31.5; $Cl_{hydrolyzable}$ 21.0; OC_3H_7 17.4. M 339.5.

Hydrolysis of the acid chloride with concd. hydrochloric acid gave a mixture of phosphorous and phosphoric acids.

Analysis of the 4th fraction gave the following results:

Found %: C 59.32, 59.37; H 10.73, 10.79; P 7.35, 7.60; OC_3H_7 38.75, 38.65. M 403.5. $C_{21}H_{25}O_6P$. Calculated %: C 59.5; H 10.6; P 7.34; OC_3H_7 41.6. M 424.

Hydrolysis of the 4th fraction by refluxing with concd. hydrochloric acid resulted in pronounced tarring of the substance and the formation of phosphoric acid (test with molybdate reagent). Evaporation of the aqueous solution in vacuo failed to yield any crystalline products.

4. Reaction of tributyl phosphite with butyraldehyde. A mixture of 1.45 g of butyraldehyde and 5 g of tributyl phosphite was heated in a sealed ampul at 140-145° for 6 hr. By repeated fractional distillation we were able to isolate 2.3 g of a fraction with the constants and the analysis given in the table for $C_{20}H_{43}O_5P$.

Hydrolysis of the substance by heating with concd. hydrochloric acid gave the crystalline (1-hydroxybutyl)-phosphonic acid with m.p. 162°.

5. Reaction of triethyl phosphite with benzaldehyde. A mixture of 8 g of triethyl phosphite and 11 g of benzaldehyde was heated in a sealed ampul at 150-160° for 6 hr. Fractional distillation led to the isolation of 1.3 g of a fraction with the constants and the analysis given in the table for $C_{13}H_{21}O_4P$.

6. Reaction of triethyl phosphite with salicylaldehyde. Proceeding in the same manner as described above, from 10 g of triethyl phosphite and 8 g of salicylaldehyde we obtained 2.1 g of a fraction with the constants and the analysis given in the table for compound No. 6, which was not investigated further.

7. Preparation of diethyl ester of methoxymethylphosphonic acid. A mixture of 12 g of triethyl phosphite and 4 g of chloromethyl methyl ether was heated in a sealed ampul at 150° for 6 hr. Here we obtained 6.0 g of the diethyl ester of methoxymethylphosphonic acid (Table, No. 7).

8. Reaction of triethyl phosphite with acrolein. Acrolein (3.4 g) was added slowly, in drops, to 10 g of triethyl phosphite in 15 ml of dry ether, after which the mixture was heated in a sealed ampul for 3 hr at 100°. We obtained 2.5 g of a fraction with the analysis and properties given in the table (No. 8).

SUMMARY

A study was made of the reaction of trialkyl phosphites with aliphatic and aromatic aldehydes and it was shown that only the aromatic aldehydes (benzaldehyde) form addition products of structure $R'CH(OR)PO(OR)_2$; acrolein adds the trialkyl phosphite in the 1,4-position. Saturated aliphatic aldehydes when reacted with trialkyl phosphites form addition products composed of two and three moles of aldehyde per mole of phosphite; the first were shown to have the structure $R'CH[OCH(OR)R']PO(OR)_2$. The addition products containing 3 moles of aldehyde do not have the organophosphorus linkage.

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THE ADDITION OF TRIALKYL PHOSPHITES TO ACRYLIC SYSTEMS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3987-3992,
December, 1960
Original article submitted July 31, 1959

In the preceding paper [1] we had shown that trialkyl phosphites react with aldehydes, forming addition products at the carbonyl group. This reaction is accompanied by condensation of the aldehydes, in which connection it was established that only aromatic aldehydes (benzaldehyde) react according to the Abramov scheme [2], while unsaturated aldehydes (acrolein) react according to the scheme of Kamai and Kukhtin [3]. It was interesting to determine if neutral phosphites are also capable of reacting with certain other classes of carbonyl compounds. It proved that under the investigated conditions the simpler ketones, for example acetone, do not react with triethyl phosphite, whereas diphenyl ketone reacts vigorously with the latter even in the cold. It was also found that triethyl phosphite does not react with diethyl oxalate, containing two conjugated C = O bonds, even at temperatures up to 170°.

The reactivity of the trialkyl phosphites toward compounds having the carbonyl group in a carboxyl group found in conjugation with an unsaturated C = C bond was investigated by us on the examples of the esters of acrylic and methacrylic acid.

In these cases it was naturally assumed that it is also possible for reaction to take place along the conjugated system C = C−C = O or across the C = C double bond, which was described on many examples of other nucleophilic compounds of trivalent phosphorus−the phosphines [4], while for the phosphites this was demonstrated by Pudovik on the example of their addition to allenes [5].

The trialkyl phosphites were reacted with the esters of acrylic and methacrylic acid by heating at 140-160° for several hours in the presence of a small amount of hydroquinone, preventing the polymerization of the acrylates. The principal products of the reaction of triethyl and tributyl phosphite with methyl acrylate are clear colorless oils, which on hydrolysis form the same tribasic organophosphorus acid with m.p. 167°, in its melting point and properties identical with the phosphonopropionic acid described many times earlier [6-8]. The infrared spectra* of the obtained esters show that the investigated compounds contain the carbonyl group (ν 5.8 μ), the P = O group (ν 8.0 μ), the P−OC (ν 10.40 μ) and PO−C (ν 9.8 μ) groups, and also the ester group C−O (ν 8.55 μ). In the infrared spectra of some of the samples weakly defined absorption bands were found in the regions of the O−H (2.8 μ) and C = C (6.2-6.3 μ) bonds, which, however, disappeared when the fractions were washed with bromine water, and consequently are due to the presence of small amounts of impurities.

These spectroscopic data, combined with the analysis results for C, H, P, and OR (three alkoxy groups) and the molecular weight, and also a comparison of the constants of the isolated products with those of compounds described in the literature [9, 7, 12], conclusively indicate that the obtained substances are respectively the triethyl and tributyl esters of phosphonopropionic acid $(RO)_2P(O)CH_2CH_2COOR$. The triethyl ester of phosphonopropionic acid, prepared by us for comparison by the reaction of triethyl phosphite with acrylic acid [10], had

*We wish to thank S. S. Dubov, who was kind enough to analyze the infrared spectra of the compounds described in this paper.

the same constants, analysis, and infrared spectral characteristics as the reaction product of triethyl phosphite with methyl acrylate. In a similar manner, the reaction of triethyl phosphite with methyl methacrylate yields the triethyl ester of phosphonoisobutyric acid $(RO)_2P(O)CH_2CH(CH_3)COOR$, while reaction with acrylonitrile yields the ester of phosphonopropionitrile $(RO)_2P(O)CH_2CH_2CN$, identified by the analysis and constants, corresponding to those given in the literature [8, 11], and also by its hydrolysis to phosphonopropionic acid. The obtained results primarily indicate that phosphites do react with acrylic systems, reacting predominantly with the unsaturated C = C bond, and not with the carbonyl or nitrile groups.

The formation of phosphonopropionic acid derivatives (or of phosphonoisobutyric acid derivatives in the case of methyl methacrylate), containing phosphite and not methyl radicals in the carboxyl groups, when methyl acrylate or methyl methacrylate reacted with either triethyl or tributyl phosphite can be explained by simultaneously progressing transesterification [13, 14]. As a matter of fact, in the reaction of butyl acrylate with triethyl phosphite, where difficulty could be expected in exchanging the butyl radical by the lighter ethyl group, the obtained ester had two ethoxy and one butoxy group. Since the trialkyl phosphites used in our work were carefully purified from dialkyl phosphites and the possibility, for example, of the reaction

$$(RO)_2P(O)H + CH_2{=}CHCO_2R' \longrightarrow (RO)_2P(O)CH_2CH_2CO_2R'$$

was excluded, then the conversion of the acrylic and methacrylic esters to phosphorus-containing propionic and isobutyric acid derivatives when reacted with trialkyl phosphite proved to be somewhat unexpected.

Together with the indicated compounds, the reaction of triethyl phosphite with methyl acrylate also yields higher boiling addition products of two and even three moles of the acrylate to one mole of the phosphite and, besides this, p-diethoxybenzene.

Since phosphites do not display a tendency to alkylate alcohol and phenols and, for example, p-diethoxybenzene is not formed when triethyl phosphite is reacted with hydroquinone (see EXPERIMENTAL) or with aldehydes in the presence of hydroquinone [1], it is possible to assume that the investigated reaction proceeds by a radical mechanism.

As a matter of fact, p-diethoxybenzene was obtained in nearly quantitative yield when methyl acrylate was reacted with triethyl phosphite in the presence of substantial amounts of hydroquinone ($\frac{1}{2}$ mole per mole of acrylate). At the same time the yield of the phosphonopropionic ester increased and high boiling polymers were completely absent in the reaction products.

The possibility of radicals taking part in the reactions of the trialkyl phosphites has been mentioned many times recently [15-20]. In the reaction discussed by us it is possible to assume, for example, that the primary addition product of trialkyl phosphite to acrylate (A) exhibits radical properties. This addition product cleaves a hydrogen atom from the hydroquinone (B) and becomes stabilized, eliminating the alkyl radical (C).

$$(RO)_3\dot{P} + CH_2{=}CHCOOR' \longrightarrow (RO)_3\dot{P}CH_2\dot{C}HCOOR' \qquad (A)$$

$$(RO)_3\dot{P}CH_2\dot{C}HCOOR' + \text{HQ} \longrightarrow (RO)_3\dot{P}CH_2CH_2COOR' + \text{Q} \qquad (B)$$

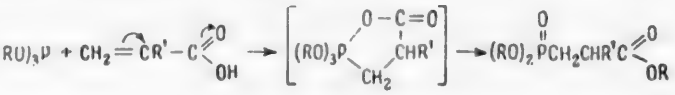
$$(RO)_3\dot{P}CH_2CH_2COOR' \longrightarrow \dot{R} + (RO)_2P(O)CH_2CH_2COOR' \qquad (C)$$

$$\dot{R} + \text{Q} \longrightarrow \text{HQ}' \text{ etc.}$$

Here the formation of polymeric addition products takes place in accordance with the scheme

$$(A) + n(CH_2{=}CHCOOR') \longrightarrow (RO)_3\dot{P}[CH_2CH(COOR')]_nCH_2\dot{C}HCOOR' \longrightarrow$$
$$\longrightarrow (RO)_2P(O)[CH_2CH(COOR')]_nCH_2CH_2COOR' + R.$$

In recent years the reaction of trialkyl phosphites with acrylic and methacrylic acids has been investigated by Kamai and Kukhtin [10, 21-26]. Here they observed the formation of phosphonopropionic and phosphonobutyric esters and comparatively high-molecular polymers. These authors assign an ionic mechanism to the reaction with involvement of an intermediate cyclic product.



However, if it is considered that acrylic acid under the influence of trialkyl phosphites can form esters with ease, then the possibility is not excluded that the transformations studied by these authors reduce to the reactions of the acrylates discussed in this paper.

EXPERIMENTAL

1. Reaction of methyl acrylate with triethyl phosphite. A mixture of 17.6 g of distilled methyl acrylate, 33.2 g of triethyl phosphite (distilled from Na) and 1 g of hydroquinone was heated in a sealed ampul for 6 hr at 140-150°. Repeated fractional distillation gave the following fractions: 1st, 143-145° (3 mm), 9.5 g, $n^{20}D$ 1.4330, d^{20}_{20} 1.121; 2nd 196° (3 mm), 2.5 g, $n^{20}D$ 1.4530, d^{20}_{20} 1.123; 3rd 210-215° (3 mm), 1.0 g, $n^{20}D$ 1.4675, d^{20}_{20} 1.129.

During the distillation a partial deposition of colorless crystals (1.5 g) in the condenser occurred in the case of the 1st and 2nd fractions.

a) Investigation of 1st fraction. Triethyl ester of phosphonopropionic acid.

Found %: C 45.19, 45.01; H 7.78, 7.80; P 12.65, 12.77. M 238.0.

Number of ethoxy groups 2.94, 3.06. $C_9H_{19}O_5P$. Calculated %: C 45.2; H 8.0; P 13.0. Number of ethoxy groups 3. M 238.0.

A mixture of 3 g of the 1st fraction and 15 ml of hydrochloric acid was heated under reflux for 6 hr, after which the solution was evaporated in vacuo and the obtained crystals (1.75 g) were recrystallized twice from a mixture of acetic acid and chloroform. Phosphonopropionic acid with m.p. 167° was obtained.

Found %: C 23.38, 24.40; H 4.91, 5.01. Titration with alkali: g-equiv. 157 (to methyl orange), 51.1 (to phenolphthalein). $C_3H_7O_5P$. Calculated %: C 23.4; H 4.55. M 154.

Treatment of 0.5 g of the above obtained acid in alcohol solution with 1 ml of aniline gave the aniline salt of phosphonopropionic acid, m.p. 158° (decomp.).

Found %: C 43.74; H 6.06; N 5.58. $C_9H_{14}O_5NP$. Calculated %: C 43.7; H 5.5; N 5.65.

A portion of the 1st fraction (2.7 g) was added to 12 g of PCl_5 and on conclusion of heat evolution the mixture was heated on the water bath for 1 hr. Then SO_2 was passed into the reaction mixture until all of the crystals had gone into solution. Fractional distillation gave us 1.3 g of the dichloride of the ethyl ester of α-Cl-phosphonopropionic acid.

B.p. 145° (3 mm), $n^{20}D$ 1.4870, d^{20}_{20} 1.419.

Found %: C 24.59, 24.88; H 3.54, 3.57; P 12.48, 12.77; Cl_{total} 39.51, 39.34; $Cl_{hydrolyzable}$ 30.31, 29.73; OC_2H_5 18.5, 18.30. $C_5H_8O_3PCl_3$. Calculated %: C 23.7; H 3.15; P 12.7; Cl_{total} 42.25; $Cl_{hydrolyzable}$ 28.0; OC_2H_5 17.8.

b) Investigation of 2nd fraction. Adduct of 2 moles of methyl acrylate and 1 mole of triethyl phosphite.

Found %: C 49.85, 50.03; H 8.11, 8.04; P 9.09, 9.34; total number of CH_3O and C_2H_5O groups 3.94, 3.94. M 323. $C_{14}H_{27}O_7P$. Calculated %: C 49.8; H 8.25; P 9.18; number of RO groups 4.0. M 338.

Hydrolysis of the 2nd fraction with hydrochloric acid gave phosphoric acid.

c) Investigation of 3rd fraction. Adduct of 3 moles of methyl acrylate and 1 mole of triethyl phosphite.

Found %: C 52.08, 52.20; H 7.93, 7.72; P 5.13, 5.05. M 398.5. $C_{18}H_{33}O_9P$. Calculated %: C 51.0; H 7.8; P 7.35. M 424.

Hydrolysis of the fraction with hydrochloric acid gave phosphoric acid.

d) Investigation of crystals. Recrystallization from aqueous alcohol gave p-diethoxybenzene with m.p. 72°.

Found %: C 72.20, 72.80; H 8.81, 8.35; OC_2H_5 55.3, 55.24. $C_{10}H_{14}O_2$. Calculated %: C 72.3; H 8.45; OC_2H_5 54.2.

2. Reaction of methyl acrylate with stoichiometric amount of hydroquinone. Operating in the same manner as before, a mixture of 8.0 g of triethyl phosphite, 4.0 g of methyl acrylate and 2.7 g of hydroquinone was heated. On fractional distillation, besides partially recovered starting materials, we obtained: 1st fraction, b.p. 142-145° (3 mm), 4.5 g, $n^{20}D$ 1.4335, d^{20}_{20} 1.125, and 2.8 g of crystals with m.p. 72°, from their analysis and properties corresponding respectively to the triethyl ester of phosphonopropionic acid and p-diethoxybenzene, and also 1.8 g of a 2nd fraction with b.p. 65.70° (2 mm), $n^{20}D$ 1.4160, and d^{20}_{20} 1.025, being the diethyl ester of ethylphosphonic acid.

Found %: C 42.39, 43.46; H 9.17, 9.28; OC_2H_5 55.35, 55.55. $C_6H_{15}O_3P$. Calculated %: C 43.2; H 9.05; OC_2H_5 54.0.

3. Reaction of acrylic acid with triethyl phosphite. A mixture of 2 g of distilled acrylic acid and 5 g of triethyl phosphite was heated under reflux on the water bath for 5 hr. On fractional distillation we obtained 3.1 g of the triethyl ester of phosphonopropionic acid.

B.p. 137-142° (3 mm), $n^{20}D$ 1.4330, d^{20}_{20} 1.119.

Found %: C 45.14, 45.23; H 7.29, 7.08; P 12.69, 12.66; OC_2H_5 54.42, 53.95. M 233. $C_9H_{19}O_5P$. Calculated %: C 45.2; H 8.0; P 13.0; OC_2H_5 56.8. M 238.

Crystals of phosphonopropionic acid with m.p. 167° were obtained when the compound was hydrolyzed with hydrochloric acid. The mixed melting point with the crystals from Expt. 1a was not depressed.

4. Reaction of acrylic acid with tripropyl phosphite. In the same manner as the preceding, from 17 g of tripropyl phosphite and 6.5 g of acrylic acid we obtained 4.5 g of the tripropyl ester of phosphonopropionic acid.

B.p. 136° (1 mm), $n^{20}D$ 1.4315, d^{20}_{20} 1.041.

Found %: C 51.20, 50.90; H 9.60, 8.65; P 10.88. M 290. $C_{12}H_{25}O_5P$. Calculated %: C 51.75; H 8.91; P 11.1. M 281.

Hydrolysis of the fraction with hydrochloric acid gave phosphonopropionic acid with m.p. 167°.

Reaction between the ester with b.p. 136° (1 mm) and phosphorus pentachloride. A mixture of 2 g of the fraction and 10 g of PCl_5 was heated on the water bath for 1 hr, after which SO_2 was passed into the mixture until the precipitate dissolved. After two fractional distillations we obtained 0.5 g of a partially decomposing fraction with b.p. 140° (1 mm), $n^{20}D$ 1.5030. This corresponds to the dichloride of the propyl ester of dichlorophosphonopropionic acid.

Found %: C 21.25, 21.52; H 2.48, 2.57; P 11.25, 11.06; Cl 47.46, 46.81; OC_3H_7 20.03, 19.67. $C_6H_9O_3PCl_4$. Calculated %: C 23.7; H 2.98; P 10.5; Cl 45.8; OC_3H_7 19.6.

5. Reaction of triethyl phosphite with hydroquinone. A mixture of 4.5 g of triethyl phosphite and 2.5 g of hydroquinone was heated in a sealed ampul for 15 hr at 140-150°. On fractional distillation we isolated 2.2 g of crystals with m.p. 168-169° (from alcohol), which corresponds to hydroquinone. p-Diethoxybenzene was not found.

6. Reaction of butyl acrylate with triethyl phosphite. A mixture of 5.0 g of triethyl phosphite, 3.85 g of butyl acrylate and 0.5 g of hydroquinone was heated in a sealed ampul for 6 hr at 140-150°. On fractional distillation we isolated 2.75 g of the diethyl butyl ester of phosphonopropionic acid with b.p. 165° (3 mm), $n^{20}D$ 1.4370, and d^{20}_{20} 1.065.

Found %: C 48.45, 48.59; H 8.84, 8.97; P 10.18, 10.90. Total number of C_2H_5O and C_4H_9O groups 2.8. M 255. Calculated %: C 49.70; H 8.60; P 11.65. Number of alkoxy groups 3.0. M 266.

Hydrolysis of the ester with hydrochloric acid gave phosphonopropionic acid with m.p. 167.5°.

7. Reaction of methyl acrylate with tributyl phosphite. In the same manner as the preceding, from 3 g of methyl acrylate and 9 g of tributyl phosphite in the presence of 0.3 g of hydroquinone we obtained 2.7 g of the tributyl ester of phosphonopropionic acid.

B.p. 140-145° (1 mm), $n^{20}D$ 1.4460, d^{20}_{20} 1.0740.

Found %: C 56.62, 56.47; H 9.69, 9.72; P 9.94, 9.56. Number of C_4H_9O groups 2.93, 2.90. M 314. $C_{15}H_{31}O_5P$. Calculated %: C 56.0; H 10.1; P 10.15. Number of C_4H_9O groups 3.0. M 322.

Hydrolysis of the ester with hydrochloric acid gave phosphonopropionic acid with m.p. 167°.

8. Reaction of triethyl phosphite with methyl methacrylate In the same manner as before, from 4 g of hydroquinone we obtained 3.2 g of the triethyl ester of phosphonoisobutyric acid.

B.p. 138-140° (2 mm), $n^{20}D$ 1.4400, d^{20}_{20} 1.1320.

Found %: C 47.26, 47.13; H 8.01, 8.06; OC_2H_5 51.50, 51.70. M 245. $C_{10}H_{21}O_5P$. Calculated %: C 47.0; H 8.35; P 12.3; OC_2H_5 53.5. M 252.

9. Reaction of triethyl phosphite with acrylonitrile. In the same manner as before, from 5.3 g of acrylonitrile, 16 g of triethyl phosphite and 0.3 g of hydroquinone we obtained 2 g of a substance, corresponding to the liethyl ester of phosphonopropionitrile.

B.p. 128° (2 mm), $n^{20}D$ 1.4370, d^{20}_{20} 1.092.

Found %: C 45.36, 45.55; H 7.24, 7.09; P 14.65, 14.76; OC_2H_5 46.71, 46.70. M 185. $C_7H_{14}O_3NP$. Calculated %: C 44.0; H 7.35; P 16.2; OC_2H_5 47.0. M 191.

Hydrolysis of the substance with hydrochloric acid gave phosphonopropionic acid, which was isolated as the aniline salt with m.p. 152° (decomp.).

Found %: C 42.41, 42.24; H 5.95, 6.17; N 6.46; P 11.46. $C_9H_{14}O_5NP$. Calculated %: C 43.7; H 5.5; N 5.65; P 12.7.

SUMMARY

It was shown that the esters and the nitrile of acrylic acid, and also methyl methacrylate, react with trialkyl phosphites to give phosphonopropionic or phosphonoisobutyric acid derivatives, respectively. The mechanism of the reaction was discussed, and it was considered to be of the free-radical type.

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THIOSULFONIC ACIDS

V. SYNTHESIS AND ANTIMICROBIAL PROPERTIES OF SOME ALKYL ESTERS OF BENZENETHIOSULFONIC ACID AND ITS DERIVATIVES*

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3993-3998, December, 1960
Original article submitted January 11, 1960

The alkyl esters of aromatic thiosulfonic acids and, in particular, of benzenethiosulfonic acid and its derivatives (I), have hardly been described in the literature. Still these compounds could possess practical interest as new antimicrobials, since their related alkyl esters (II) of alkanethiosulfonic acids exhibit a broad spectrum of antimicrobial action and in experiments in vitro show considerable activity toward gram-positive, gram-negative and acid-resistant bacteria, various fungi, etc. [2].

(I) (II)

Of special interest is the action of esters (II) on phytopathogenic bacteria and fungi, responsible for plant diseases: the use of these esters for the pretreatment of the seeds of various grain, vegetable and technical cultures sharply reduces their susceptibility to disease and at the same time stimulates growth of the plants, shifting the phases of their development toward early ripening, giving in the final analysis a substantial increase in the productivity [3]. It is also possible to expect esters (I) to have a similar action.

For this reason we undertook in the present paper the synthesis of some alkyl esters of benzenethiosulfonic acid and its derivatives (I) by the method employed earlier for the synthesis of the analogous esters of alkanethiosulfonic acids, namely, by the reaction of potassium thiosulfonates with alkyl bromides in accordance with the reaction (1).

$$Ar-SO_2-SK + AlkBr \rightarrow Ar-SO_2-S-Alk + KBr \quad (1)$$

The potassium salts of the thiosulfonic acids were obtained by reacting the corresponding acid chlorides with an aqueous solution of potassium hydrosulfide.

The potassium thiosulfonates listed in Table 1, with the exception of No. 5, are colorless crystalline compounds, readily soluble in water, soluble in boiling ethyl and butyl alcohols, and insoluble in benzene, chloroform, ether and other organic solvents. The potassium salt of p-nitrobenzenethiosulfonic acid is yellow and is much less soluble in water. Salts Nos. 2, 3 and 5 are new compounds.

Reaction (1) was run in aqueous acetone solution at room temperature with constant shaking, since heating on the water bath gave deeply colored products. However, at room temperature this reaction goes very slowly, especially with the isopropyl and isobutyl bromides; the length of holding at room temperature also determines

*The work was reported at the Fourth Ukrainian Republican Conference on Organic Chemistry [1].

TABLE 1

Potassium Salts of Arenethiosulfonic Acids $Ar-SO_2-SK$

Expt. No.	Ar	M.p.	Sulfur content (in %)		Yield (in %)	Crystal form (from alcohol)
			found	calc.		
1	C_6H_5	212°	30.34	30.20	70.7	Rectangular prisms
2	$p\text{-}ClC_6H_4$	Does not melt up to 270	25.84	25.99	70.0	Tetragonal plates
3	$p\text{-}CH_3OC_6H_4$	218	26.21	26.46	73.1	Long needles
4	$p\text{-}CH_3CONHC_6H_4$	256	23.65	23.81	70.1	Dense hexahedral plates
5	$p\text{-}NO_2C_6H_4$	256—257 (with decomp.)	24.93	24.92	60.0	Rectangular plates

the yields of the final products. Thus, in the case of obtaining the isopropyl ester of benzenethiosulfonic acid (Table 2, No. 4) the yield of ester was 30% for a reaction time of 120 hr, and 60% for a reaction time of 480 hr; in this connection we were able to isolate the esters in a high state of purity, nearly colorless, and not requiring further purification.

Esters 1-18 (Table 2) were isolated as slightly yellow oily liquids; they fail to distill without decomposition at a vacuum of 1-2 mm, but can be distilled at a higher vacuum, and here they were obtained as colorless oily liquids with a weak specific odor of onion or garlic.*

The molecular refractions of these esters, calculated from the atomic refractions [4], differ substantially from the experimental values, exceeding the possible experimental errors. This, however, cannot be explained by an insufficient purity of the obtained products, which was verified by us by special control experiments: some of the esters during distillation under a high vacuum were separated into individual fractions, despite the fact that they all distilled at a constant temperature; the refractive index and the density were determined for each of these fractions. They proved to be so close among themselves that the molecular refractions calculated from these constants differed among themselves by a matter of only hundredths.

It is obvious that the additive scheme does not take into account the reciprocal influence of the atoms, and also the presence of conjugation between the benzene ring and its substituents. This also explains the fact that for each series of esters the deviations of the experimental molecular refractions from the calculated are values of the same order and when additional corrections (exaltations) are introduced all of the calculated molecular refractions lie close to the experimental values.

For the esters of benzenethiosulfonic acid this correction should be taken equal to 0.4, for the esters of p-chlorobenzenethiosulfonic acid equal to 1.1, and for the esters of p-methoxybenzenesulfonic acid equal to 1.6.

The other arenethiosulfonic esters listed in Table 2 (Nos. 19-31) are crystalline compounds; the alkyl esters of acetylthiosulfanilic acid (Nos. 19-25), after repeated recrystallization from 40% alcohol, were obtained as

*For this reason we were somewhat surprised to see in a recent communication [13] the statement that the ethyl ester of p-bromobenzenethiosulfonic acid has b.p. 158° at 2-3 mm. As described above, we synthesized potassium p-bromobenzenethiosulfonate, isolated it in the pure state as colorless crystals, not melting when heated to 270°, and by reacting it with ethyl bromide at room temperature we obtained and isolated in the pure state the ethyl ester of p-bromobenzenethiosulfonic acid, the constants of which are given in Table 2 (No. 32). It proved that this ester also does not distill at 1-2 mm without decomposition; it is purified by distillation in a high vacuum at a residual pressure of 10^{-4} mm, but even at 10^{-2} mm it darkens rapidly when heated and cannot be distilled without decomposition.

TABLE 2

Alkyl Esters of Benzenethiosulfonic Acid and Its Derivatives $Ar-SO_2-S-Alk$

Expt. No.	Ar	Alk	M.p.	B.p. (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.*	ΔMR_D	Sulfur content (%) found	Sulfur content (%) calc.	Yield (in %)**	Reaction time (in hr)
1	C_6H_5	C_2H_5	—	90—91° (10^{-4})	1.2555	1.5736	53.134	52.823	0.311	31.64, 31.62	31.70	68.4	120
2	C_6H_5	C_3H_5	—	95—95.5 (10^{-3})	1.2438	1.5814	57.447	56.974	0.473	30.01	29.92	78.7	0.5
3	C_6H_5	C_3H_7	—	94—95 (10^{-4})	1.2125	1.5627	57.913	57.441	0.472	29.67	29.65	59.9	120
4	C_6H_5	iso-C_3H_7	—	84—84.5 (10^{-4})	1.2092	1.5603	57.867	57.441	0.426	29.60	29.65	30.0, 64.1	120, 480
5	C_6H_5	C_4H_9	—	96—97 (10^{-4})	1.1819	1.5547	62.529	62.059	0.470	27.67	27.84	64.2	120
6	C_6H_5	iso-C_4H_9	—	86—87 (10^{-4})	1.1840	1.5561	62.547	62.059	0.488	27.50	27.84	20.6	180
7	p-$CH_3OC_6H_4$	C_2H_5	—	120—121 (10^{-4})	1.2777	1.5813	60.624	59.084	1.540	27.43	26.61	75.1	120
8	p-$CH_3OC_6H_4$	C_3H_5	—	108—109 (10^{-3})	1.2380	1.5711	64.855	63.235	1.620	26.15	26.23	72.0	0.5
9	p-$CH_3OC_6H_4$	C_3H_7	—	115—116 (10^{-4})	1.2393	1.5717	65.376	63.702	1.674	26.09	26.03	61.4	120
10	p-$CH_3OC_6H_4$	iso-C_3H_7	—	104—105 (10^{-4})	1.2345	1.5691	65.383	63.702	1.681	26.14	26.03	26.2	180
11	p-$CH_3OC_6H_4$	C_4H_9	—	112—113 (10^{-4})	1.2057	1.5623	70.060	68.420	1.640	24.56	24.63	66.3	120
12	p-$CH_3OC_6H_4$	iso-C_4H_9	—	110—111 (10^{-4})	1.2068	1.5626	70.033	68.420	1.613	24.45	24.63	29.8	180

*The same as in previous papers [2], the refractions of the $>SO_2$ group and of sulfide sulfur $-S-$ were taken equal to 8.63 and 8.00, respectively (average values); the exaltation of the grouping $-SO_2-S-$ was taken equal to + 0.6.

**Alkyl esters Nos. 1–18 were each distilled 2 to 3 times in a high vacuum; the losses in the distillations were to 10–25% (the latter applying to the isopropyl and isobutyl esters).

TABLE 2 (Cont'd)

Expt. No.	Ar	Alk	M.p.	B.p. (pressure in mm)	d_{20}^{20}	n_D^{20}	MR_D found	MR_D calc.	ΔMR_D	Sulfur content (%) found	Sulfur content (%) calc.	Yield (in %)	Reaction time (in hr)
13	p-ClC_6H_4	C_2H_5	—	113—114 (10^{-4})	1.3589	1.5886	58.676	57.690	0.986	27.22	27.09	59.8	120
14		C_3H_5	—	103—104 (10^{-3})	1.3393	1.5930	62.514	61.841	1.092	25.66	25.78	66.9	0.5
15		C_3H_7	—	111 (10^{-3})	1.3120	1.5781	63.441	62.308	1.133	25.51	25.57	51.9	120
16		iso-C_3H_7	—	93—94 (10^{-3})	1.3087	1.5764	63.448	62.308	1.140	25.43	25.57	17.7	420
17		C_4H_9	—	101.5—102 (10^{-4})	1.2718	1.5683	68.149	66.926	1.223	24.00	24.21	47.2	120
18		iso-C_4H_9	—	92—93 (10^{-4})	1.2752	1.5694	68.069	66.926	1.143	24.19	24.21	26.8	180
19	p-$CH_3CONHC_6H_4$	C_2H_5	88°	—	—	—	—	—	—	24.69	24.72	67.9	48
20		C_3H_5	60	—	—	—	—	—	—	23.45	23.63	66.6	2
21		C_3H_7	47—48	—	—	—	—	—	—	23.37	23.45	44.2	48
22		iso-C_3H_7	113—114	—	—	—	—	—	—	23.38	23.45	17.0	48
23		C_4H_9	76	—	—	—	—	—	—	22.29	22.31	42.3	2 with heating
24		iso-C_4H_9	80	—	—	—	—	—	—	22.19	22.31	12.5	48
25		$CH_2BrCHBrCH_2$	121—122	—	—	—	—	—	—	14.81	14.87	34.6	—
26	p-$NO_2C_6H_4$	C_2H_5	75—76	—	—	—	—	—	—	24.02	24.21	45.8	20 with heating
27		C_3H_5	45—46	—	—	—	—	—	—	24.59	24.74	49.6	4
28		C_3H_7	59—60	—	—	—	—	—	—	24.41	24.52	31.0	20
29		iso-C_3H_7	168—169	—	—	—	—	—	—	24.35	24.52	17.7	60
30		C_4H_9	66—67	—	—	—	—	—	—	23.12	23.12	43.0	20 with heating
31		iso-C_4H_9	57—58	—	—	—	—	—	—	22.94	23.12	17.3	60
32	p-BrC_6H_4	C_2H_5	23—24	115—116 (10^{-4})	1.5896	1.6066	61.058	60.588	0.47	22.76, 22.92	22.81	50.0	480

colorless products. They tend to separate from solution as oily liquids that crystallize with great difficulty. The alkyl esters of p-nitrobenzenethiosulfonic acid (Nos. 26-31) were also purified by recrystallization from 40% alcohol and were isolated as colorless crystals; some of the esters have a pale yellow color.

All of the alkyl esters of the arenethiosulfonic acids are very difficultly soluble in water, and are readily soluble in alcohol, acetone, ether, and other organic solvents; most of them are new compounds (with the exception of Nos. 1, 20 and 25 [5, 6]).*

A study of the antimicrobial activity of the alkyl esters of benzenethiosulfonic acid and its derivatives, carried out in the Institute of Microbiology of the Academy of Sciences of the Ukrainian SSR, revealed** that in their bacteriostatic and fungistatic properties these compounds resemble esters (II) very closely; being somewhat inferior to the latter in their antibacterial action, they retain a fairly substantial activity only toward certain fungi.

Alkyl esters (I) are also inferior to the analogous esters of the alkanethiosulfonic acids in their action on phytopathogenic bacteria, but in individual cases they exhibit a very high activity, especially toward bacteria of the Xanthomonas species.

A study of the action of these compounds on the seeds of various agricultural cultures, made by K. I. Bel'tyukova and co-workers, revealed that the esters of the thiosulfonic acids are not only harmless to the tissues of perennial leguminous grasses and grain and vegetable cultures, but they also promote enhanced germination and an increase in the weight and size of the shoots, and they also sharply reduce the number of diseased plants.

The field experiments also confirmed the high effectiveness of certain alkyl esters of the arenethiosulfonic acids on commercial tracts; their use as agents for the pretreatment of the seeds of grain, vegetable and technical cultures gives a sharp reduction in the susceptibility of these plants to disease and a substantial increase in the productivity, which makes it possible to propose the esters (I) for practical use in agriculture [7].

EXPERIMENTAL***

The acid halides of the sulfonic acids were obtained in conventional manner – by the chlorosulfonation of chlorobenzene, anisole, and acetanilide [8, 9]; p-nitrobenzenesulfonyl chloride was prepared by the action of wet chlorine on p-nitrothiophenol in acetic acid medium [10]. The melting points of the products after their purification agreed with the literature data [8-12].

The potassium salts of the arenethiosulfonic acids were synthesized by reacting the sulfonyl chlorides with aqueous potassium hydrosulfide solution, in the same manner as the earlier described salts of the alkanethiosulfonic acids were prepared [2].

We found that the potassium salt of p-nitrobenzenethiosulfonic acid could not be obtained and isolated under these conditions, since pronounced tarring of the product occurred. However, by using more dilute potassium hydrosulfide solution, obtained by saturating a solution of potassium hydroxide in water, taken in a 1 : 8 ratio, with hydrogen sulfide, to synthesize the thiosulfonate we were able to avoid secondary reactions. The end product was also isolated in a different manner than the other thiosulfonates: after adding the p-nitrobenzenesulfonyl chloride to the potassium hydrosulfide solution and heating the reaction mass until the separated elemental sulfur had dissolved, the solution was treated with activated carbon, filtered, and crystals of the potassium salt of p-nitrobenzenethiosulfonic acid deposited from the filtrate, which were filtered and then recrystallized twice from water; evaporation of the filtrate gave an additional amount of the salt.

The alkyl esters of the arenethiosulfonic acids were obtained by reacting the potassium thiosulfonates with alkyl bromides in acetone medium at room temperature or with heating on the water bath (see Table 2), in the same manner as the alkyl esters of the alkanethiosulfonic acids were synthesized [2].

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*The ethyl ester of benzenethiosulfonic acid (Table 2, No. 1), obtained earlier [5], was not distilled and its physicochemical constants were not given, and the same is true for the potassium benzenethiosulfonate (Table 1, No. 1).

**We take this opportunity to thank V. G. Drobot'ko, B. E. Aizenman and S. I. Zelepukhe for the microbiological testing of the esters of the thiosulfonic acids. We also sincerely thank K. I. Bel'tyukova and co-workers for the major study of several years duration made by them on the antimicrobial activity of these compounds and the effectiveness of their use under field conditions.

***Students L. I. Pavlenko and Z. M. Poshivak assisted in the work.

SUMMARY

1. By reacting the sulfonyl chlorides with potassium hydrosulfide we obtained and identified 6 potassium salts of arenethiosulfonic acids, including 3 not described in the literature.

2. We synthesized 32 alkyl esters of the arenethiosulfonic acids; 28 of them are new compounds.

3. The antimicrobial action of the alkyl esters of the arenethiosulfonic acids was characterized; it was observed that these compounds show a high activity toward phytopathogenic bacteria and also exert a stimulating effect on the development of plants, which made it possible to propose some of the esters for practical use in agriculture.

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REACTION OF ALIPHATIC DINITRILES WITH GLYCOLS AND HYDROGEN CHLORIDE

E. N. Zil'berman and A. E. Kulikova

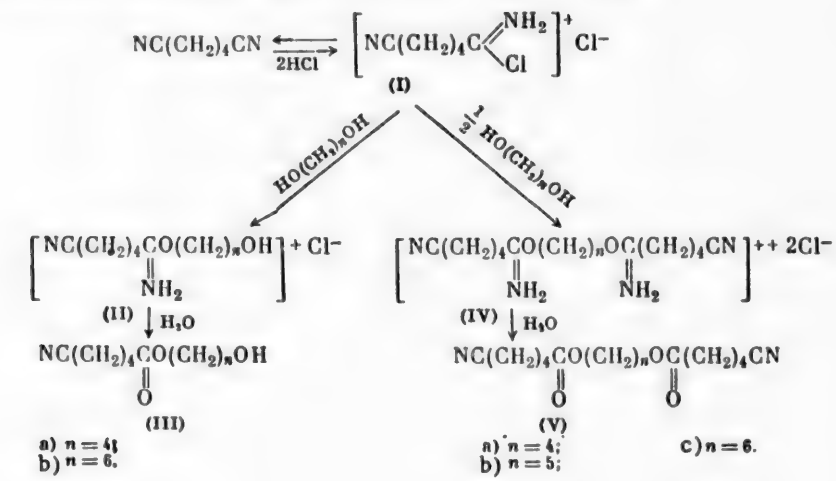
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 3999-4002, December, 1960
Original article submitted February 8, 1960

It was shown by us recently that at the start in the hydrochlorination of adiponitrile two molecules of HCl add selectively to one nitrile group. Only when the hydrochlorination is continued does the second nitrile group enter into reaction [1]. From the reaction product of adiponitrile and hydrogen chloride, taken in a 1 : 2 molar ratio (apparently δ-cyanovalerimidochloride hydrochloride [1]), and an equivalent amount of primary alcohol we obtained in high yield the hydrochlorides of the alkyl imido ethers of δ-cyanovaleric acid, which on hydrolysis are converted to the corresponding esters of δ-cyanovaleric acid [2].

Little information exists in the literature on the preparation of imido ethers from glycols. Attempts to synthesize the salts of imido ethers from glycols, nitriles and hydrogen chloride in the presence and in the absence of solvents failed to give the desired results until recently [3]. It was only recently that a paper appeared on the preparation of the hydrochlorides of diimido ethers from cyanogen, ethylene glycol and hydrogen chloride [4].

In this paper we studied the reaction of adiponitrile and sebaconitrile with hydrogen chloride and a number of diprimary glycols, namely 1,4-butanediol, 1,5-pentanediol, and 1,6-hexanediol.

The reaction of compounds (I) with equivalent amounts of the glycols gave the corresponding imido-ether hydrochlorides (II), which were obtained as viscous materials. Hydrolysis of the latter gave the hydroxybutyl [n = 4, (IIIa)] and hydroxyhexyl [n = 6, (IIIb)] esters of δ-cyanovaleric acid.



Characteristics of Obtained Esters

Compound	Yield (%)	M.p.	Mol. wt. found	Mol. wt. calc.	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Found, % C	Found, % N	Found, % H	Empirical formula	Calculated % C	Calculated % N	Calculated % H
(IIIa)	80	—	192*	199	1.4588	1.0791	50.41	51.38	59.92	6.92	8.29	$C_{10}H_{17}O_3N$	60.30	7.03	8.54
(IIIb)	98	36°	235	227	—	—	—	—	64.42	6.03	9.25	$C_{12}H_{21}O_3N$	63.43	6.17	9.25
(Va)	97	—	300	308	1.4643	1.0891	78.32	79.03	61.75	8.90	7.76	$C_{16}H_{24}O_4N_2$	62.33	9.09	7.76
(Vb)	98	—	317	322	1.4579	1.0546	83.29	83.65	63.31	8.83	8.08	$C_{17}H_{26}O_4N_2$	63.35	8.69	8.07
(Vc)	82	—	320	336	1.4521	1.0263	88.33	88.27	63.61	8.05	8.40	$C_{18}H_{28}O_4N_2$	64.28	8.33	8.33
(VIIIa)	96	—	272*	290	1.4660	1.1042	72.70	73.21	57.65	—	8.71	$C_{14}H_{26}O_6$	57.90	—	8.96
(VIIIb)	92	19.5	326*	318	1.4695	1.0674	83.03	82.89	60.36	—	9.13	$C_{16}H_{30}O_6$	60.28	—	9.43
(VIIIc)	84	24	323*	346	1.4605**	1.0438**	90.86	91.68	62.27	—	9.84	$C_{18}H_{34}O_6$	62.42	—	9.82
(VIIId)	82	45	350*	346	—	—	—	—	62.56	—	9.77	$C_{18}H_{34}O_6$	62.42	—	9.82

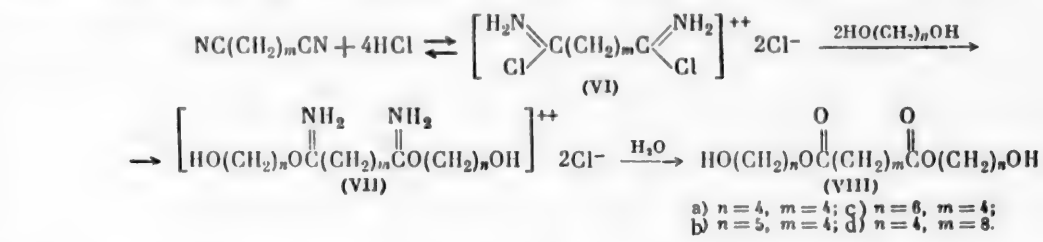
*Based on active hydrogen content.

**Determined at 25°.

The treatment of compounds (I) with a 0.5 molar amount of α,ω-glycols gave in a similar manner, through the imido-ether salts (IV), the di(δ-cyanovalerates) of 1,4-butanediol [n = 4, (V a)], 1,5-pentanediol [n = 5, (V b)] and 1,6-hexanediol [n = 6, (V c)].

Compounds of type (III) and (V) could not be isolated from the reaction products of sebaconitrile, HCl and glycols, taken in the molar ratios 1 : 2 : 1 and 1 : 2 : 0.5. This is explained by the fact that the selectivity reactivity of one nitrile group is absent in the case of sebaconitrile [5].

The reaction of adiponitrile or sebaconitrile with hydrogen chloride in a molar ratio of at least 1 : 4 gave us solid products, apparently diimidochloride dihydrochlorides (VI), which precipitated when insufficient solvent was used. Without isolation from the reaction mixture, the latter were treated with double molar amounts of the glycols. The formed diimido-ether hydrochlorides (VII) with excess water gave the ω,ω'-dihydroxybutyl [n = 4, m = 4, (VIII a)], ω,ω'-dihydroxypentyl [n = 5, m = 4, (VIII b)] and ω,ω'-dihydroxyhexyl [n = 6, m = 4, (VIII c)] esters of adipic acid and the ω,ω'-dihydroxybutyl ester of sebacic acid [n = 4, m = 8, (VIII d)].



a) n = 4, m = 4; c) n = 6, m = 4;
b) n = 5, m = 4; d) n = 4, m = 8.

All of the compounds synthesized by us in the present paper (Table) are new. They are oligomers relative to the recently obtained low-molecular polyesters with terminal nitrile and alcohol groups [6].

EXPERIMENTAL

Synthesis of di(4-hydroxybutyl) ester of adipic acid (VIII a). A heterogeneous mixture of 10.8 g of adiponitrile and 25 ml of absolute ether was saturated at 0-5° with 20 g of dry hydrogen chloride. A colorless precipitate of adipodiimidochloride dihydrochloride (VI) deposited when the mixture was stirred for 2 hr with cooling. The reaction mixture was then treated with 18 g of 1,4-butanediol and the stirring was continued for another 4-5 hr. Here the chloride (VI) went into solution, after which the reaction mixture stratified, and the lower layer was soon converted to a viscous mass. After removal of the solvent in vacuo, the imido-ether salt (VII) contained a substantial amount of adsorbed hydrogen chloride (found Cl 25-26%, instead of the calculated 19.5%). For this reason the salt (VII) was treated with an amount of caustic solution equivalent to the total hydrogen chloride, for which the compound (VII) was dissolved in 140 ml of 2.5% NaOH solution. After 2 hr a lower oily layer separated. This layer was removed, while the water layer was extracted with ethyl acetate. The extracts and oily layer were combined, and then dried over anhydrous sodium sulfate. After removal of the solvent we obtained 28 g (96.5%) of ester (VIII a), which was identified as the bis(α-naphthylurethan), m.p. 75°.

Found %: N 4.22. $C_{36}H_{40}O_8N_2$. Calculated %: N 4.45.

The other glycols (VIII) were obtained in a similar manner.

The synthesis of the hydroxynitriles (III) and dinitriles (V) and their isolation was accomplished in the same manner as described above for glycol (VIII a), except that the glycol was added to the reaction mixture after at least 4 hr from the time of passing in the hydrogen chloride.

SUMMARY

1. Methods were developed for the synthesis of the ω,ω' dihydroxyalkyl esters of dibasic acids and the previously unknown hydroxyalkyl esters of δ-cyanovaleric acid and di(δ-cyanovalerates) of α,ω-glycols.

2. Nine representatives of the indicated classes of compounds were synthesized.

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1,5-DIARYL-3-HALOFORMAZANS

I. SYNTHESIS OF MONO- AND DIHALO-SUBSTITUTED DERIVATIVES OF 1,5-DIPHENYL-3-CHLOROFORMAZAN

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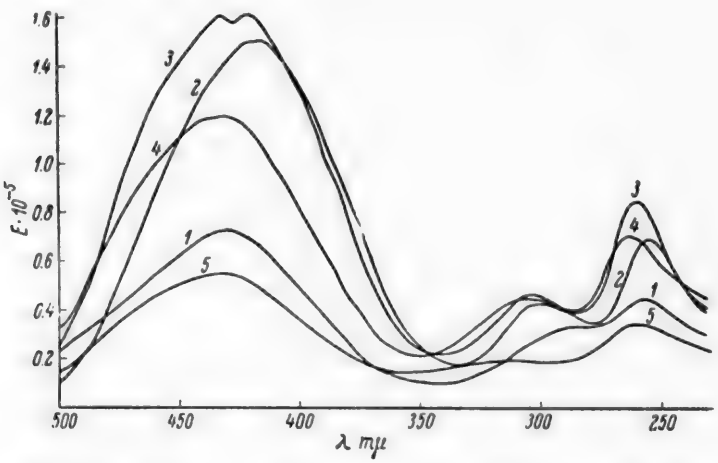
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4002-4005, December, 1960
Original article submitted February 8, 1960

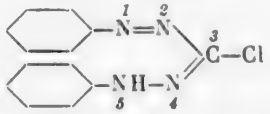
Derivatives of 1,5-diaryl-3-chloroformazan, containing phenyl, p-tolyl, p-nitrophenyl and β-naphthyl radicals, are described in the literature [1]. 1,5-Diphenyl-3-iodoformazan was obtained by the exchange reaction of 1,5-diphenyl-3-chloroformazan and potassium iodide, with heating in acetone solution [1]. Attempts to effect a similar exchange with potassium bromide proved unsuccessful. Unsymmetrical derivatives of 1,5-diphenyl-3-chloroformazan have also been synthesized [2]. Bromination of the diphenylformazan with bromine in glacial acetic acid gave 1,5-di(p-bromophenyl)-3-bromoformazan [3].



Absorption spectra of alcohol solutions of 1,5-diphenyl-3-chloroformazan derivatives. 1) 1,5-Diphenyl-3-chloroformazan (with 4×10^{-5} M); 2) 1,5-di(p-fluorophenyl)-3-chloroformazan (with 5×10^{-5} M); 3) 1,5-di(p-chlorophenyl)-3-chloroformazan (with 5×10^{-5} M); 4) 1,5-di(p-bromophenyl)-3-chloroformazan (with 4×10^{-5} M); 5) 1,5-di(p-iodophenyl)-3-chloroformazan (with 2×10^{-5} M).

Statements exist on the antitubercular properties of carbazides of thioaldonic acids, obtained from formazans containing carbohydrate moieties [4], and on the biological activity of formazans in which the phenyl rings are substituted with quaternary ammonium groups [5].

1,5-Diaryl-3-chloroformazans of General Formula



Name of 3-chloroformazan	Yield (%)	M.p.	Max. absorption (mμ)	Min. absorption (mμ)	Found %	Empirical formula	Calc. %, N
1,5-Di(o-fluorophenyl)-3-chloroformazan	48	125—126° (from aqueous dioxane)	246, 290, 420	280, 335	19.40, 19.31	$C_{13}H_9N_4F_2Cl$	19.01
1,5-Di(m-fluorophenyl)-3-chloroformazan	72	132—133 (from 1:2 dioxane–alcohol mixture)	252, 417	335	18.85, 18.78	$C_{13}H_9N_4F_2Cl$	19.01
1,5-Di(p-fluorophenyl)-3-chloroformazan	72	175—176 (from aqueous dioxane)	254, 298, 417	278, 335	18.86, 18.83	$C_{13}H_9N_4F_2Cl$	19.01
1,5-Di(o-chlorophenyl)-3-chloroformazan	71	178—179 [2]	253, 305, 413	284, 335	—	$C_{13}H_9N_4Cl_3$	17.10
1,5-Di(p-chlorophenyl)-3-chloroformazan	64	194—195 (from 1:1 alcohol–acetone mixture)	260, 305, 421, 432	285, 343, 426	16.79, 16.72	$C_{13}H_9N_4Cl_3$	17.10
1,5-Di(o-bromophenyl)-3-chloroformazan	75	195—196 (from aqueous acetone)	255, 302, 420	284, 332	13.16, 13.07	$C_{13}H_9N_4ClBr_2$	13.45
1,5-Di(m-bromophenyl)-3-chloroformazan	77	198—199 (from aqueous acetone)	254, 300, 417	285, 330	13.33, 13.30	$C_{13}H_9N_4ClBr_2$	13.45
1,5-Di(p-bromophenyl)-3-chloroformazan	61	200—202 (from acetone–alcohol mixture)	262, 306, 430,	285, 350	13.51, 13.44	$C_{13}H_9N_4ClBr_2$	13.45
1,5-Di(o-iodophenyl)-3-chloroformazan	55	200.5—201.5 (from aqueous dioxane)	255, 300, 425	295, 390	11.35, 11.23	$C_{13}H_9N_4ClI_2$	10.97
1,5-Di(m-iodophenyl)-3-chloroformazan	66	155—156 (from aqueous dioxane)	262, 425	340	10.80, 10.79	$C_{13}H_9N_4ClI_2$	10.97
1,5-Di(p-iodophenyl)-3-chloroformazan	76	194—197 (from aqueous dioxane)	262, 315, 433	295, 360	10.62, 10.61	$C_{13}H_9N_4ClI_2$	10.97
1,5-Di(2,4'-dichlorophenyl)-3-chloroformazan	78	206—206.5 (from aqueous dioxane)	263, 305, 440	275, 355	14.20, 14.09	$C_{13}H_7N_4Cl_5$	14.13
1,5-Di(2',4'-dibromophenyl)-3-chloroformazan	71	237.5—238 (from aqueous dioxane)	252, 310, 430	292, 348	9.95, 9.92	$C_{13}H_7N_4ClBr_4$	9.75
1,5-Di(2',5'-dichlorophenyl)-3-chloroformazan	89	244—245 (from aqueous dioxane)	254, 423	330	14.32, 14.29	$C_{13}H_7N_4Cl_5$	14.13
1,5-Di(2',5'-dibromophenyl)-3-chloroformazan	66	261—262 (from dioxane)	260, 425	340	9.65, 9.49	$C_{13}H_7N_4ClBr_4$	9.75

(Continued)

Name of 3-chloroformazan	Yield (%)	M.p.	Max. absorption (mμ)	Min. absorption (mμ)	Found % N	Empirical formula	Calc. % N
1,5-Di(2',3'-dichlorophenyl)-3-chloroformazan	53	165—167° (from dioxane)	257, 425	350	14.11, 14.02	$C_{13}H_7N_4Cl_5$	14.13
1,5-Di(3',4'-dichlorophenyl)-3-chloroformazan	96	147—149 (from dioxane)	264, 430	365	14.19, 14.09	$C_{13}H_7N_4Cl_5$	14.13
1,5-Di(2'-chloro-5'-trifluoromethylphenyl)-3-chloroformazan	59	179—180 (from alcohol–dioxane mixture)	262, 294, 415	285, 330	11.91, 11.81	$C_{15}H_7N_4F_6Cl_3$	12.16

The substituted formazans proved to be suitable as chelating agents for various cations [6-9].

For this reason it seemed of interest to synthesize a number of mono- and dihalo-substituted derivatives of 1,5-diphenyl-3-chloroformazan. We obtained these compounds by reacting derivatives of benzenediazonium chloride with the dipotassium salt of chloromalonic acid in aqueous solution containing sodium acetate.

$$2[RN{\equiv}N]^+\bar{Cl} + ClCl(CO_2K)_2 \xrightarrow{CH_3CO_2Na} \begin{matrix} RN{=}N \\ \diagdown \\ C{-}Cl \\ \diagup \\ RNH{-}N \end{matrix} + 2KCl + 2CO_2$$

The properties of the synthesized compounds are given in the table.

The mono- and dihalo-substituted derivatives of the 1,5-diaryl-3-chloroformazans are crystalline products, often with a metallic luster, having either a yellow-orange or a red-orange color. They are readily soluble in dioxane, acetone, chloroform and pyridine, less readily soluble in benzene, alcohol and carbon tetrachloride, and insoluble in water.

The absorption spectra of alcohol solutions of the 1,5-diphenyl-3-chloroformazan derivatives synthesized by us were taken using an SF-4 spectrophotometer at 5 mμ intervals along the curve, and at 2 mμ intervals in the extreme regions of absorption. From a portion of the obtained absorption curves it can be seen (Figure) that in going from the p-fluoro to the p-iodo derivative of 1,5-diphenyl-3-chloroformazan, a bathochromic shift of 8 mμ is observed in the 250-265 mμ region and one of 15 mμ in the 410-440 mμ region.

EXPERIMENTAL

We obtained the starting o-, m- and p-fluoroanilines from the corresponding nitroanilines through the fluoborates of the diazo compounds [10], with their subsequent decomposition to the fluoronitrobenzenes and reduction to the corresponding amines [11].

o-Iodoaniline was obtained by the Baeyer method [12]. The 2,5-dichloro- and 2,5-dibromoanilines were obtained by the nitration of the corresponding p-dichloro- and p-dibromobenzenes [13] and reduction of the nitro derivatives with iron in hydrochloric acid medium, analogous to the reduction of 2-chloro-5-trifluoromethylnitrobenzene [14].

Chloromalonic ester and the dipotassium salt of chloromalonic acid were obtained by the Irving and Bell method [3].

The substituted 3-chloroformazan derivatives were obtained by the general method given below for the o-fluoro derivative.

1,5-Di(o-fluorophenyl)-3-chloroformazan. A solution of 3 g of o-fluoroaniline in 15 ml of 12% hydrochloric acid was diazotized at 0° with a solution of 2.2 g of sodium nitrite in 5 ml of water. The solution was filtered and the filtrate was poured rapidly into a cooled stirred solution of 2.9 g of potassium chloromalonate and 5.8 g of sodium acetate in 15 ml of water. The solution turned turbid at first, then became yellow, and finally assumed a red color. Carbon dioxide was evolved. The mixture was stirred at 0° for 8 hr, then for 2 hr at room temperature, diluted with 150 ml of water, and stirred for another hour. The obtained red precipitate was filtered, washed on the filter several times with water, and dried in the air. Yield 1.9 g. After recrystallization from aqueous acetone the compound was obtained as red-orange crystals with a metallic luster.

SUMMARY

Seventeen new mono- and dihalo-substituted derivatives of 1,5-diphenyl-3-chloroformazan were synthesized and the absorption spectra of their alcohol solutions were measured.

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QUINOLINE AND ITS DERIVATIVES

XXVII.* CO-CONDENSATION OF GLYCERALDEHYDE AND 3-PHENYLGLYCERALDEHYDE WITH AROMATIC AMINES

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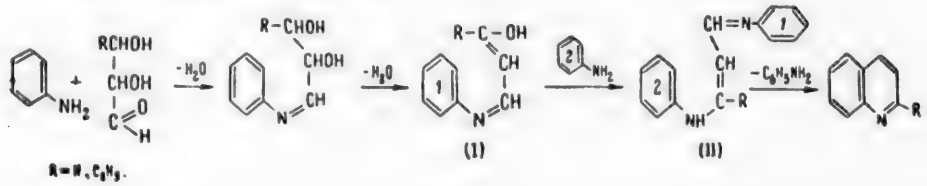
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4005-4007, December, 1960
Original article submitted February 8, 1960

It was indicated earlier that besides acrolein, it is possible for glyceric and hydracrylic (β-hydroxypropionic) aldehydes to take part in the Skraup synthesis [1]. The important role of hydracrylaldehyde in the mechanism of the Skraup reaction was shown recently [2-4]. The experimental results obtained in the present paper on the reaction of diphenylamine with acrolein in acid medium serve to confirm these observations. The impossibility of obtaining N-phenylquinolinium salts by this method is evidence against the possible scheme of aromatic amines reacting with hydracrylaldehyde where the latter is first dehydrated to acrolein.

We were also unable to obtain N-phenylquinolinium salts when we attempted to cyclize 1,3-bis(diphenylamino)propene, obtained by the reaction of acrolein with diphenylamine in neutral medium [5], under various conditions. This fact, as well as a number of other facts discussed earlier [6], contradicts the theory that dianils of hydracrylaldehyde and β-hydroxyacrolein may be the principal intermediate products of the Skraup reaction [7].

In running the Skraup synthesis it is possible for glyceraldehyde, formed in the oxidation of glycerol by mild oxidizing agents, which role can be played by nitroaromatic compounds [8], to be formed in the reaction medium. We studied the reaction of glyceraldehyde and 3-phenylglyceraldehyde with aromatic amines under various conditions. Quinoline is obtained in small yield when glyceraldehyde, taken as the diethyl acetal, is added to aniline in concd. sulfuric acid at 100-140°. We were unable to isolate the quinoline base when aniline was replaced by p-anisidine.

Instead of the possible 4-phenylquinoline, the reaction of 3-phenylglyceraldehyde with aniline in the presence of sulfuric acid yields 2-phenylquinoline, which was also obtained from the anil of 3-phenylglyceraldehyde [6, 9]. The yield can be increased somewhat if an excess of aniline is used. The mechanism for the formation of the quinoline bases is depicted in accordance with the scheme [6]:



*See Zhur. Obshchei Khim. Nos. 1, 4, 9 and 11 (1959) and No. 5 (1960), and also Uchenye Zapiski Rostov na Don Gosudarst. Univ., No. 10 (1959).

The formation of malonaldehyde dianil (II) from the monoanil (I) may also be depicted by the scheme of disproportionation of the latter into malonaldehyde and its dianil [10]. Quinoline [10] was obtained in 9-15% yield from malonaldehyde monoanil (Claisen compound), which agrees with the results of our experiment.

The low yield of quinoline bases is explained by the fact that methylglyoxal monoanils [11], which polymerize with ease, are formed in the dehydration of the glyceraldehyde anils.

EXPERIMENTAL

Reaction of diphenylamine with acrolein. For reaction we took 34 g of diphenylamine, 30 g of nitrobenzene and 36 g of concd. H_2SO_4. This mixture was heated to 100° and then 12 ml of acrolein was added in drops, after which the temperature was raised to 140° and kept at this level for 1-1.5 hr. The product was isolated in the same manner as described previously [12]. We obtained 10-13 g of colorless crystals with m.p. 167°, and analyzing 6.80% nitrogen.

In different experiments, depending on the ratios of the starting products and the reaction time, the melting points of the obtained products ranged from 152 to 167°. Replacement of the acrolein by glycerol gave similar products with m.p. 148-154°. The structure of these products was not established.

Quinoline. Five milliliters of concd. H_2SO_4 was added to 4 g of aniline with cooling and then 3.6 g of glyceraldehyde diethyl acetal [13] was added gradually in 15-20 min at 80-100°, after which the mixture was kept at 100° for 1 hr. The free bases were isolated by steam distillation from alkaline solution, while the tertiary amines were precipitated with potassium ferrocyanide [14]. Quinoline was isolated as the picrate from saturated alcohol solution. The yield of the picrate was 1.28 g (8.3%). M.p. 200°. The mixed melting point with authentic quinoline picrate was not depressed.

2-Phenylquinoline. For reaction we took 4 g of aniline, 6 ml of concd. H_2SO_4 and 10 g of 3-phenylglyceraldehyde diethyl acetal. The reaction was run in the same manner as in the synthesis of quinoline. The free base was extracted with ether, and removal of the ether by evaporation left the 2-phenylquinoline as a crystalline product. Yield 0.54 g (6.1%), m.p. 79-80°.

Found %: N 6.69. $C_{15}H_{11}N$. Calculated %: N 6.82.

Picrate, m.p. 188°.

3-Phenylglyceraldehyde anil. A yellow crystalline precipitate began to deposit immediately when 3.1 g of aniline was mixed with 8 g of 3-phenylglyceraldehyde diethyl acetal. M.p. 96-97° (from alcohol).

Found %: N 5.63. $C_{15}H_{15}O_2N$. Calculated %: N 5.83.

2-Phenylquinoline from the anil. To 6.3 g of 3-phenylglyceraldehyde anil was added 1.8 g of aniline and 6 ml of concd. H_2SO_4. The temperature was raised gradually to 140° and then kept at 140° for 1 hr. The free base was isolated by extraction with ether. Yield 0.42 g (10.3%). M.p. 79°.

Picrate, m.p. 189°.

SUMMARY

1. The results of the experiments on the reaction of diphenylamine with acrolein confirm the scheme for the formation of quinolines from aromatic amines and hydracrylaldehyde.

2. It was established that glyceraldehyde and 3-phenylglyceraldehyde when reacted with aniline form quinolines in 7-10% yield, as a result of which this reaction, in contrast to the reaction with hydracrylaldehyde, apparently has little importance for the mechanism of the Skraup reaction.

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INTERACTION OF 3-FURANIDONES WITH DIAZOMETHANE

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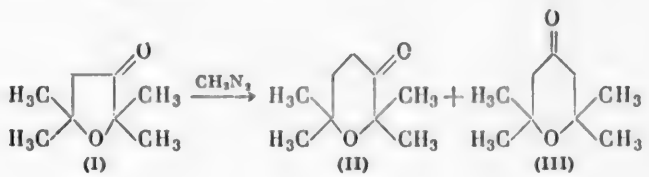
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4008-4016, December, 1960
Original article submitted January 11, 1960

Ring expansion of carbocyclic ketones under the action of diazomethane has been amply investigated, whereas, relatively little attention has been paid to the expansion of heterocyclic ketones. It was shown [1] that tetrahydro-4-thiapyrone is smoothly converted by diazomethane in situ into a 1 : 1 mixture of 1-thiacyclo-4-heptanone and 4-methylenetetrahydrothiapyran in a total yield of 82%. Ring expansion of tetrahydro-4-pyrone goes with very great facility under the action of an ethereal solution of diazomethane ex situ with formation of 1-hydroxy-4-cyclopentanone (60%) and 4-methylenetetrahydropyran (23%) [2]. Treatment of 1-benzyl-4-piperidone with diazomethane in situ gives 1-benzyl-1-azacyclo-4-pentanone (38%) [3]. Ring expansion of five-membered heterocyclic ketones has not been studied. Very little work also has been done on ring expansion of five-membered carbocyclic ketones. All that we know in this field is that cyclopentanone reacts with diazomethane to give a mixture of cycloheptanone, α-oxides, and cyclooctanone [4].

We reported previously [5] that 2,2,5,5-tetramethyl-3-furanidone undergoes ring expansion when treated with diazomethane, and forms a mixture of the isomeric 2,2,6,6-tetramethyltetrahydro-3-pyrone (II) and 2,2,6,6-tetramethyltetrahydro-4-pyrone (III).

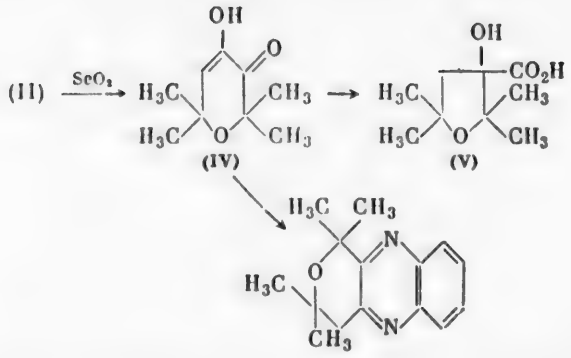


For resolution of this mixture we took advantage of the ability of the tetrahydropyrone (III) to react with sodium bisulfite [6]; the tetrahydropyrone (II), containing only one α-methylene group, does not react.

For expansion of the ring of the furanidone (I) we utilized an ethereal solution of diazomethane [4], N-nitroso-N-methylurea [7], N-nitroso-N-methylurethane [8], and N-nitroso-N-methylurethylane. The table shows that the best reagent for ring expansion of the furanidone (I) is N-nitroso-N-methylurethane; very similar results, however, are obtained with N-nitroso-N-methylurethylane. We are the first to use the latter for ring expansions.

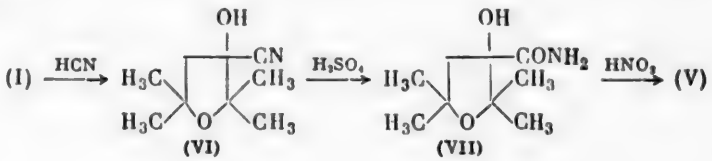
Compound (II) predominates considerably in the resulting mixture of tetrahydropyrones, compound (III) being present only in traces. No difficulties arise in the separation of the minute quantities of (III), so that this reaction can be recommended as a method of synthesis of 2,2,6,6-tetramethyltetrahydro-3-pyrone (II), a representative of the class of tetrahydro-β-pyrones which has scarcely been studied (the only member to be described in the literature is 2,2-diphenyltetrahydro-3-pyrone [9]).

In order to verify the structure of tetrahydropyrone (II), we oxidized it with selenium dioxide and obtained Δ^4-2,2,6,6-tetramethyldihydro-3-pyrone-4-ol (IV).



The ultraviolet spectrum of compound (IV) had λ_{max} 265 mμ, log ε 3.92 (in methanol), in good agreement with literature data for a carbocyclic diosphenol of analogous structure: λ_{max} 266 mμ, log ε 3.90 in methanol [10]. The α-dicarbonyl structure of (IV) was also confirmed by preparation of the quinoxaline derivative – 2,2,4,4-tetramethyltetrahydro-(3,4-b)-pyranoquinoxaline.

By benzyl rearrangement of the diosphenol (IV) we obtained 3-hydroxy-2,2,5,5-tetramethylfuranidine-3-carboxylic acid (V); we also synthesized it by another route [11] from the furanidone (I) via the cyanohydrin (VI) and the amide (VII).



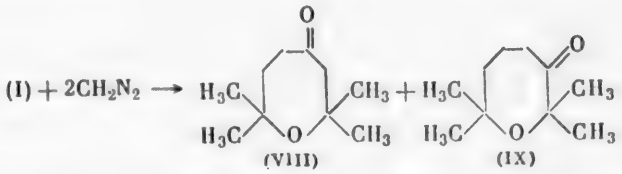
It may be noted that hydroxynitrile (VI) and amide (VII) had higher melting points than were recorded in [11] (7 and 20° higher respectively). Their solubility was also higher than previously reported. By cleavage of amide (VII) with nitrous acid we obtained a hydroxyacid identical with the hydroxyacid (V) prepared from the diosphenol (IV). These reactions demonstrated the presence of a six-membered oxygen-containing ring in compound (II). Additional evidence was an intense absorption band with a frequency of 1726 cm^{-1} in the infrared spectrum of tetrahydropyrone (II). This band is characteristic of the carbonyl group in six-membered cyclic ketones [12].

Yields of 2,2,6,6-Tetramethyltetrahydro-3-pyrone (II) and 2,2,6,6-Tetramethyltetrahydro-4-pyrone (III)

Method	Source of diazomethane	% excess of diazomethane	% of unchanged furanidone (I)	Yield of mixture of tetrahydropyrones (II) and (III) (%)		Content of (III) in mixture (%)	Yield of high-boiling residue in % of weight of mixture of tetrahydropyrones (II) and (III)
				on the furanidone (I) introduced	on furanidone (I) consumed		
ex situ	CH_2N_2	21	54.5	18.5	41.0	2.6	
in situ	$CH_3N(NO)CONH_2$	0	52.0	10.5	22.5		
		150	24.5	20.0	28.0	1.2	210
		200	14.0	17.0	20.0		170
in situ	$CH_3N(NO)CO_2C_2H_5$	0	43.0	33.0	58.0		32
		5.7	35.0	34.0	52.5		41
in situ	$CH_3N(NO)CO_2CH_3$	5.0	46.5	29.5	55.5	1.5	
		38	35.0	35.5	55.0		63

The second compound formed from furanidone (I) by treatment with diazomethane – 2,2,6,6-tetramethyltetrahydro-4-pyrone (III) – has been described in the literature. Its oxime (m.p. 101°) [6] and semicarbazone (m.p. 212°) [13] have also been described. Our semicarbazone of the tetrahydropyrone (III) had m.p. 220°. We therefore, prepared (III) from phorone, as described in [13], but again the semicarbazone melted at 220°, and there was no depression in a mixed melting point test with the semicarbazone of tetrahydropyrone (III) prepared by expansion of the ring of furanidone (I).

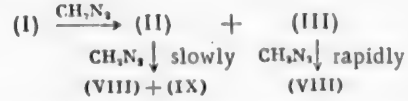
The high-boiling fractions remaining after separation of tetrahydropyrones (II) and (III) were treated with sodium bisulfite. By decomposition of the bisulfite derivative we then obtained the pure seven-membered ketone (VIII) – 1-oxa-2,2,7,7-tetramethyl-4-cyclopentanone (26% of the weight of all the high-boiling fractions); treatment of the aqueous solution with semicarbazide gave a mixture of semicarbazones (~ 30%). By fractional crystallization of this mixture was isolated the semicarbazone of the seven-membered ketone (IX); decomposition of the latter gave the seven-membered ketone (IX) – 1-oxa-2,2,7,7-tetramethyl-3-cyclopentanone (6.3% of the weight of the high-boiling fractions).



It should be noted that cyclic ketones (I), (II), (III), (VIII), and (IX) form semicarbazones at different rates: ketones (III) and (VIII) (lacking substituents in the α-position to the carbonyl) form them instantaneously when the reactants are mixed in the cold; ketones (I), (II), and (IX) (with two methyl groups at the carbon adjacent to the carbonyl) only form them after heating or after prolonged standing. The inhibiting effect in the ketones of the second group is undoubtedly due to screening of the ketonic group by the two methyls.

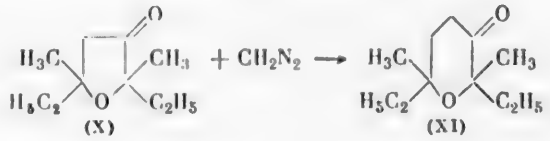
An interesting feature of our experiments on ring expansion of 2,2,5,5-tetramethyl-3-furanidone by treatment with diazomethane is that one of the possible isomers – tetrahydropyrone (II) – is formed almost exclusively. The reason for this must be sought in the relative reactivities of compounds (II) and (III), since it has been established that the direction of expansion of aromatic ring-substituted 2-arylcyclohexanones does not depend on the nature of the substituent in the aromatic ring, i.e., it does not depend on the electronic character of the substituent in the α-position of the cyclic ketone.

The first step in our reaction of furanidone (I) with diazomethane is ring expansion with formation of comparable quantities of tetrahydropyrones (II) and (III). In respect of the character of the environment of the carbonyl group, tetrahydropyrone (II) resembles furanidone (I), and therefore to a first approximation (neglecting the influence of the size of the ring) it must interact with diazomethane at a speed approximating to the speed of its interaction with furanidone (I), which reacts sluggishly with diazomethane (see table). Consequently the resulting tetrahydropyrone (II) does not undergo further substantial changes, and we separated the greater part of it from the reaction mixture. Nevertheless its ring does undergo expansion to a minute extent, as reflected in the presence of the seven-membered ketone (IX) in the higher-boiling fractions.

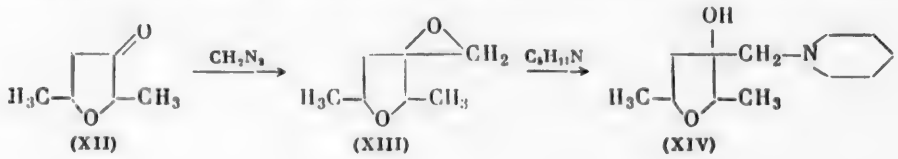


A different reactivity is exhibited by tetrahydropyrone (III) which lacks substituents at the carbon atom adjacent to the carbonyl group. In this respect it resembles tetrahydro-4-pyrone which is known to react with very great facility with diazomethane to give an expanded ring [2]. The second step is therefore ring expansion of the resulting tetrahydropyrone (III) under the action of diazomethane to form the seven-membered ketone (VIII), a considerable quantity of which (up to 26%) was isolated from the high-boiling fraction of the reaction product.

The homolog of furanidone (I)–2,5-dimethyl-2,5-diethyl-3-furanidone (X)–reacts very much more sluggishly with diazomethane: from the reaction mixture was isolated 2,6-dimethyl-2,6-diethyltetrahydro-3-pyrone (XI)* [37% on the furanidone (X) consumed and 6.5% on the furanidone brought into reaction]; under these conditions 2,6-dimethyl-2,6-diethyltetrahydro-4-pyrone is not formed at all.



The reaction of the lower homolog of furanidone (I)–2,5-dimethyl-3-furanidone (XII)–with diazomethane goes very much more energetically than that of furanidone (I) [only 21% of unchanged furanidone (XII) was isolated], but it leads to a complex mixture from which only 3-methylene-2,5-dimethylfuranidine oxide (XIII) could be isolated, in negligible yield. Compound (XIII) was identified through the derived aminoalcohol (XIV).



EXPERIMENTAL

Sublimation was effected in a 2-3 mm vacuum. Semicarbazones were prepared by the normal procedure [15]. N-Nitroso-N-methylurethylane was prepared by nitrosation of N-methylurethylane by a procedure similar to that used for nitrosation of N-methylurethane [16]. Phorone was synthesized by the method of [17] as modified by Kazantsev [18].

2,2,6,6-Tetramethyltetrahydro-3-pyrone (II) and 2,2,6,6-tetramethyltetrahydro-4-pyrone (III). To a well-stirred suspension of 1 g of freshly calcined, finely pulverized potassium carbonate in a solution of 42.6 g of furanidone (I) (b.p. 147-149° at 755 mm, $n^{20}D$ 1.4202) [19] in 80 ml of absolute methanol was added dropwise in the course of 7 hr 39.6 g of N-nitroso-N-methylurethane at 15-20°. The mixture was left overnight. Addition of 300 ml of absolute ether was followed (half an hour later) by separation of the precipitate. The ether was distilled from the filtrate and the methanol was distilled in vacuo; the latter was redistilled, and the residues were combined and fractionated in vacuo. The following were obtained: a) 18.25 g (43%) of unchanged furanidone (I), b.p. 59-64° (29 mm), $n^{19}D$ 1.4200; b) 15.5 g of a mixture of tetrahydropyrones (II) and (III), b.p. 72.5-74.5° (18 mm), $n^{19}D$ 1.4410; c) 5 g of high-boiling residue.

The mixture of tetrahydropyrones (II) and (III) was diluted with 100 ml of ether and shaken for 2-3 days with 200 ml of concentrated sodium bisulfite solution. The ethereal layer was separated and the aqueous layer thoroughly extracted with ether. The ether was driven off from the combined extracts (after drying with potassium carbonate), and the residue distilled to give pure tetrahydropyrone (II) in the form of a colorless liquid with a camphor odor.

M.p. 6-7°, b.p. 62-63° (9 mm), $n^{20}D$ 1.4413, d^{20}_4 0.9529, MR_D 43.32; calc. 43.22.

Found %: C 69.20, 69.26; H 10.49, 10.44. $C_9H_{16}O_2$. Calculated %: C 69.19; H 10.32.

Semicarbazone: colorless needles with m.p. 197-198° (from water).

Found %: N 19.53, 19.73. $C_{10}H_{19}O_2N_3$. Calculated %: N 19.70.

Benzylidene derivative. A mixture of 500 mg of tetrahydropyrone (II), 680 mg of benzaldehyde, 1 ml of 20% sodium hydroxide solution, and 10 ml of alcohol was left for a week at 20°, after which the alcohol was taken off in vacuo. Treatment of the residue with boiling water gave an oil which crystallized on cooling. Colorless crystals, m.p. 79-80° (from aqueous alcohol).

Found %: C 78.50, 78.64; H 8.40, 8.39. $C_{16}H_{20}O_2$. Calculated %: C 78.65; H 8.25

*Tetrahydropyrone (XI) was prepared in the analytically pure state by decomposition of its 2,4-dinitrophenylhydrazone with pyruvic acid.

The bisulfite solution together with the solid bisulfite compound (if the latter had come down) were decomposed with excess of solid potassium or sodium carbonate and thoroughly extracted with ether. To the residue (after the ether had been removed) were added 500 mg of semicarbazide hydrochloride and 750 mg of sodium acetate in the minimum quantity of water. Tetrahydropyrone (III) semicarbazide came down; m.p. 219-220° [decomp., measured after insertion in a block heated to 205° (from water)]; lustrous scales; the literature [13] gives m.p. 212° (decomp.).

Found %: N 19.64, 19.58. $C_{10}H_{19}O_2N_3$. Calculated %: N 19.70.

1-Oxa-2,2,7,7-tetramethyl-4-cyclopentanone (VIII) and 1-oxa-2,2,7,7-tetramethyl-3-cyclopentanone (IX). The high-boiling residues from all the experiments (61.7 g) were distilled in vacuo, and the 65-85° (5 mm) fraction was taken off (53.2 g) and shaken for three days with 150 ml of concentrated sodium bisulfite solution. The precipitate (36 g) was collected and washed with ether. The ethereal solution was separated, 150 ml of sodium bisulfite solution was added, and the mixture shaken for another three days (no precipitate). The ethereal layer was separated and the bisulfite solutions extracted with ether. The bisulfite derivative was added to the extracts and the whole decomposed with solid potassium carbonate. Ketone (VIII) was distilled with steam, the distillate saturated with potassium carbonate and extracted with ether. The ether was driven off from the extracts (after drying with magnesium sulfate), and the residue crystallized. Yield 16.1 g of ketone (VIII); colorless prisms with a camphor odor, m.p. 20.5-21.5° (from n-hexane at −70° and after distillation in vacuo); b.p. 68-69° (2 mm), $n^{20}D$ 1.4587 (in the supercooled state).

Found %: C 70.43, 70.29; H 10.54, 10.59. $C_{10}H_{18}O_2$. Calculated %: C 70.54; H 10.66.

Semicarbazone: lustrous, lamellar crystals, m.p. 199° (from aqueous alcohol).

Found %: N 18.77, 18.63. $C_{11}H_{21}O_2N_3$. Calculated %: N 18.49.

The combined ethereal solutions that remained after separation of the bisulfite derivative were dried with potassium carbonate, the ether was driven off, and the residue fractionated in vacuo to give the following fractions: 1st, b.p. 65-70° (5 mm), $n^{21}D$ 1.4522, 16.85 g; 2nd, b.p. 70-75° (5 mm), $n^{21}D$ 1.4543, 3.1 g.

From the 1st fraction was obtained 6.1 g of a mixture of semicarbazones, and from the 2nd 1.63 g. Fractional crystallization from aqueous alcohol gave 5.15 g of the semicarbazone of ketone (IX); colorless crystals with m.p. 213-213.7°.

Found %: C 58.39, 58.21; H 9.33, 9.10; N 18.86, 18.69. $C_{11}H_{21}O_2N_3$. Calculated %: C 58.12; H 9.31; N 18.49.

The 5.15 g of the semicarbazone of ketone (IX) was boiled in 50 ml of saturated aqueous oxalic acid solution for 10 min, the ketone (IX) distilled with steam, and the distillate saturated with potassium carbonate and extracted with ether. The ether extracts were dried with magnesium sulfate, the ether driven off, and the residue distilled in vacuo to give 2.22 g of ketone (IX); a colorless liquid with a pleasant, characteristic odor.

B.p. 84-84.5° (3 mm), $n^{20}D$ 1.4573, d^{20}_4 0.9456, MR_D 49.06; calc. 47.83.

Found %: C 70.64, 70.50; H 10.73, 10.74. $C_{10}H_{18}O_2$. Calculated %: C 70.54; H 10.66.

2,2,6,6-Tetramethyltetrahydro-4-pyrone (III) from phorone [13]. A stream of dry hydrogen chloride was passed into 21 g of ice-cooled phorone until the weight increase was 11.8 g (calculated 11.1 g). The mass was left overnight in a refrigerator and washed four times with water. The heavy, colorless oil was separated, stirred for 3 hr with 100 ml of water at 90-95°, saturated with sodium chloride, and extracted with ether. The extracts were dried with magnesium sulfate, the ether was distilled off, and the residue fractionated in vacuo to give 1.25 g (5%) of tetrahydropyrone (III); a colorless liquid with a camphor odor, b.p. 62.5-63.5° (11 mm), $n^{20}D$ 1.4377.

Literature: b.p. 73-75° (17 mm), $n^{20}D$ 1.4540 [13], b.p. 70° (15 mm), $n^{20}D$ 1.4432 [6].

Semicarbazone: m.p. 220° (decomp.) (from aqueous alcohol). No depression in a mixed melting test with the semicarbazone of the tetrahydropyrone (III) described above.

Found %: N 19.68, 19.66. $C_{10}H_{19}O_2N_3$. Calculated %: N 19.70.

Δ^4-2,2,6,6-Tetramethyldihydro-3-pyrone-4-ol (IV). To a boiling solution of 5.6 g of selenium dioxide in 70 ml of dioxane and 2 ml of water was added, with stirring, in the course of an hour 7.8 g of tetrahydropyrone (II) in 10 ml of dioxane. The mixture was boiled for another 5 hr. The selenium was separated and washed with dioxane. After the dioxane had been distilled in vacuo, the residue was distilled. The 78-80° (11 mm) fraction crystallized. Yield 4.23 g (50%) of colorless plates (by sublimation) or colorless needles (on rapid crystallization). Soluble in caustic alkali. M.p. 69.5-70° (from ligroine at −70° and after sublimation at 70-75°).

Found %: C 63.72, 63.59; H 8.25, 8.33. $C_9H_{14}O_3$. Calculated %: C 63.51; H 8.29.

2,2,4,4-Tetramethyltetrahydro-(3,4-b)-pyranoquinoxaline. A solution of 226 mg of diosphenol (IV) and 143.5 mg of o-phenylenediamine in 1 ml of alcohol was heated for an hour on a water bath, and the solvent was taken off in vacuo. The residue crystallized when rubbed. Yield 301.5 mg of substance with m.p. 45-46° (from aqueous alcohol at −70° and sublimation at 70-80°); colorless crystals, readily soluble in organic solvents, insoluble in water. Decomposes in light.

Found %: C 74.06; H 7.41; N 11.39, 11.41. $C_{15}H_{18}ON_2$. Calculated %: C 74.35; H 7.49; N 11.56.

3-Hydroxy-2,2,5,5-tetramethylfuranidine-3-carboxylic acid (V). a) A solution of 1.25 g of potassium hydroxide in 3 ml of water was boiled for 15 min in a nitrogen stream, 510 mg of compound (IV) was added, and the mixture boiled for a further 8 hr. After cooling, the mass was acidified to pH 1 with concentrated hydrochloric acid, and the precipitate was separated and sublimed. Yield 395 mg (70%) of substance in the form of colorless needles with m.p. 156-156.7° (from ligroine and after sublimation at 107°).

Found %: C 57.56, 57.55; H 8.59, 8.52. $C_9H_{16}O_4$. Calculated %: C 57.43; H 8.57.

Methyl ester of acid (V). The ester was obtained in quantitative yield by methylation with an excess of diazomethane solution; m.p. 55.5-56.5° (after sublimation at 45-50°); colorless crystals. The ester is stable to the action of ammonia.

Found %: C 59.40, 59.54; H 9.10, 9.10. $C_{10}H_{18}O_4$. Calculated %: C 59.38; H 8.97.

b) A mixture of 7.3 g of furanidone (I), 1.7 g of anhydrous hydrocyanic acid, and four drops of 50% potassium hydroxide solution was left to stand overnight. To the crystallizing mass was added five drops of 50% sulfuric acid; the mixture was heated on a water bath and the product crystallized from alcohol. Yield 6.36 g (73%) of 3-hydroxy-3-cyano-2,2,5,5-tetramethylfuranidine (VI) [11]; m.p. 84-85° (from n-hexane and after sublimation at 60-70°); colorless needles [11].

Found %: C 64.06, 63.94; H 8.94, 8.96. $C_9H_{15}O_2N$. Calculated %: C 63.88; H 8.93.

A solution of 1.69 g of cyanohydrin (VI) in 1.06 g of 92% sulfuric acid was heated for 7 min on a boiling water bath, then dissolved in water, neutralized with solid potassium carbonate, and evaporated to dryness in vacuo. The residue was extracted with hot benzene. Removal of the benzene in vacuo left 0.98 g (52.5%) of 3-hydroxy-2,2,5,5-tetramethylfuranidine-3-carboxylic acid amide (VII) [11]; m.p. 123.4-123.9° (from isooctane); colorless crystals subliming in vacuo at 120-125°. Literature [11]: m.p. 103°.

Found %: N 7.70, 7.58. $C_9H_{17}O_3N$. Calculated %: N 7.48.

To a solution of 184 mg of amide (VII) in 2 ml of 25% sulfuric acid (heated nearly to boiling) was slowly added a solution of 156.5 mg of sodium nitrite in 1.9 ml of water from a pipet reaching to the bottom of the flask. The mixture was heated to the boil and cooled. After the lapse of 5 hr the precipitate (64 mg) was filtered; the filtrate was extracted with ether, and after distillation of the ether the dried extract yielded a further 65.5 mg. Total yield 129.5 mg (70.5%) of 3-hydroxy-2,2,5,5-tetramethylfuranidine-3-carboxylic acid (V), m.p. 155.5-156.5° (after reprecipitation from alkaline solution and sublimation in vacuo). A mixture with acid (V) obtained from diosphenol (IV) did not have a depressed melting point.

2,6-Dimethyl-2,6-diethyltetrahydro-3-pyrone (XI). Dropwise addition was made at a uniform rate of 78 g of N-nitroso-N-methylurethylane during 30 hr at 15-20° to a vigorously stirred suspension of 3 g of freshly calcined and finely pulverized potassium carbonate in 102 g of furanidone (X) (b.p. 64-65° at 5 mm, $n^{20}D$ 1.4373 [19]) in 200 ml of anhydrous methanol. The product was worked up in the usual manner to give two fractions: a) Unchanged furanidone (X) (84.25 g, 82.5%) with b.p. 63-66° at 5 mm, $n^{21}D$ 1.4368.

2,4-Dinitrophenylhydrazone; m.p. 134.5° (from alcohol).

Found %: N 15.99, 15.90. $C_{16}H_{22}O_5N_4$. Calculated %: N 15.99.

b) A fraction (9.35 g) with b.p. 81-90° at 5 mm, $n^{21}D$ 1.4500, not reacting with sodium bisulfite. Its solution in 50 ml of alcohol was added to a solution of 11 g of 2,4-dinitrophenylhydrazine in 22 ml of sulfuric acid and 100 ml of alcohol. There was obtained 14 g of the 2,4-dinitrophenylhydrazone of tetrahydropyrone (XI) with m.p. 89.5-90° (from alcohol); yellow needles.

Found %: C 56.44, 56.39; H 6.84, 6.78; N 15.36, 15.57. $C_{17}H_{24}O_5N_4$. Calculated %: C 56.03; H 6.64; N 15.38.

A mixture of 14 g of the 2,4-dinitrophenylhydrazone of (XI), 10 ml of pyruvic acid, 30 ml of acetic acid, 50 ml of chloroform, and 2 ml of concentrated hydrobromic acid was heated for 3 hr at 50-60° until crystals of the 2,4-dinitrophenylhydrazone of pyroracemic acid ceased to come down. After cooling, the crystals were separated and washed with chloroform. The filtrate was poured into a mixture of ice and salt, made strongly alkaline with sodium hydroxide solution, and extracted with ether. Ether and chloroform were taken off (after drying with potassium carbonate) and the residue distilled in vacuo to give 3.3 g (46.5%) of tetrahydropyrone (XI); a colorless liquid with a camphor odor.

B.p. 62-63° (2 mm); 91-92° (11 mm), $n^{20}D$ 1.4474, d^{20}_4 0.9432, MR_D 52.24; calc. 52.45.

Found %: C 71.77, 71.78; H 11.10, 10.94. $C_{11}H_{20}O_2$. Calculated %: C 71.69; H 10.94.

Furfurylidene derivative: A mixture of 212 mg of the tetrahydropyrone (XI), 221 mg of furfural, 0.1 ml of 20% potassium hydroxide solution, and 1 ml of alcohol was left overnight and then poured into 20 ml of water. An oil separated and was extracted with benzene; the extract was dried with potassium carbonate and chromatographed on alumina. The lower, yellow ring was eluted with anhydrous benzene, the benzene was distilled in vacuo, and the residue evaporated at 100° (5 mm); a light-yellow, viscous oil with $n^{19}D$ 1.5582.

Found %: C 73.31, 73.37; H 8.55, 8.72. $C_{16}H_{22}O_3$. Calculated %: C 73.25; H 8.45.

2,5-Dimethyl-3-methylenefuranidine oxide (XIII). To a vigorously stirred suspension of 1 g of freshly calcined and finely pulverized potassium carbonate in a solution of 22.9 g of furanidone (XII) (b.p. 57.5-59° at 30 mm, $n^{23}D$ 1.4239 [20]) in 45 ml of anhydrous methanol at 15-20° was added 26 g of N-nitroso-N-methylurethylane dropwise over a period of 6 hr. Working-up in the usual manner gave two fractions. a) A fraction of 4.9 g (21.5%) of unchanged furanidone (XII) with b.p. 53-58° (25 mm), $n^{26}D$ 1.4243; b) a 1.0 g fraction with b.p. 57-60° (20 mm), $n^{25.5}D$ 1.4292. The latter was impure oxide (XIII), a mixture of which with 2.3 ml of piperidine was boiled for 3.5 hr. Fractionation in vacuo gave 0.89 g of 3-hydroxy-2,5-dimethyl-3-(N-piperidino)methylfuranidine (XIV); a colorless oil, quickly turning yellow on standing, b.p. 101-103° (2 mm), $n^{19.5}D$ 1.4811.

Found %: C 67.82, 68.09; H 10.76, 10.87; N 6.60, 6.47. $C_{12}H_{23}O_2N$. Calculated %: C 67.56; H 10.87; N 6.57.

We convey sincere thanks to Yu. K. Yur'ev for his continued interest in our work.

SUMMARY

1. Experiments with 2,2,5,5-tetramethyl-3-furanidone and 2,5-dimethyl-2,5-diethyl-3-furanidone showed that interaction of diazomethane with five-membered heterocyclic ketones leads to formation of six-membered heterocyclic ketones, predominantly of the 2,2,6,6-tetraalkyltetrahydro-3-pyrone series.

2. The best results were obtained by using N-nitroso-N-methylurethane and N-nitroso-N-methylurethylane as the source of diazomethane. The reaction with 2,2,5,5-tetramethyl-3-furanidone can serve as a preparative route to 2,2,6,6-tetramethyltetrahydro-3-pyrone; secondary reaction products are tetraalkyloxacycloheptanones.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

TETRAALKYLFURANIDINE-3,4-DIONES IN THE SYNTHESIS OF TETRAALKYLTETRAHYDROPYRAN-3,5-DIONES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4016-4023, December, 1960
Original article submitted January 15, 1960

The reaction of diazomethane with α-dicarbonyl compounds has been studied very much less thoroughly than the reaction with monocarbonyl compounds. In some cases (even the simplest) the structure of the resulting compounds has not been strictly proven, and the reactions themselves are not generally of preparative interest.

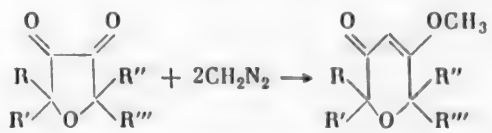
α-Dicarbonyl compounds, susceptible to enolization, either do not react with diazomethane [1] or form methyl ethers of the enolic form [1-3]. Non-enolizing α-diketones, for example aromatic α-diketones [1,4], vicinal triketones [1, 5-7], and o-quinones [1, 4, 8-14], as well as certain other α-diketones [5, 15], react with diazomethane with formation of methylenedioxy compounds or α-oxides.

There are some examples, however, of reaction of cyclic α-dicarbonyl compounds with diazomethane with ring expansion. It has thus been shown [16-18] that isatin (and substituted isatins) react with diazomethane to form a mixture of α-oxide and 2,3-dihydroxyquinoline (methylation of the latter gives in addition 2-hydroxy-3-methoxyquinoline). In addition to the usual reaction course, the methylene group of diazomethane is thus inserted between the carbonyl group and the benzene ring. Reaction of diazomethane with croconic acid gave [19] trimethoxy-p-benzoquinone, i.e., the methylene group of diazomethane is inserted between two carbonyl groups of the vicinal triketone (and methylation is subsequently effected by the excess of diazomethane).

After the present publication had gone to press, Eistert and Miller [20] reported a similar reaction of another vicinal triketone – triketohydrindan – with diazomethane.

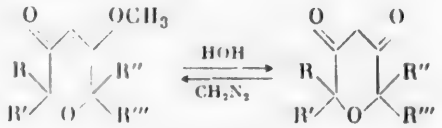
We may point out that Rupe and co-workers [21, 22] had earlier shown that camphorquinone also reacts with diazomethane with ring expansion, and methylation of the enolic forms of the resulting 2,4-homocamphordione gives a mixture of the two isomeric methyl ethers of the latter.

We established [23] that reaction of 2,2,5,5-tetraalkylfuranidine-3,4-diones with an ethereal solution of diazomethane in presence of methanol goes with expansion of the ring between the two carbonyl groups. Under the reaction conditions the resulting 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones are enolized and then methylated by the excess of diazomethane so that the products of the reaction are methyl ethers of 2,2,6,6-tetraalkyldihydro-3-pyrone-5-ols.



In the present work we showed, on the basis of experiments with a considerable number of furanidine-3,4-diones, that this reaction is a general one and proceeds with a yield of 40-50%

Methyl ethers of 2,2,6,6-tetraalkyldihydro-5-pyrone-5-ols are easily hydrolyzed by hydrochloric acid to give 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones, and they can be regenerated in nearly quantitative yield by methylation of the hydrolyzate with diazomethane.

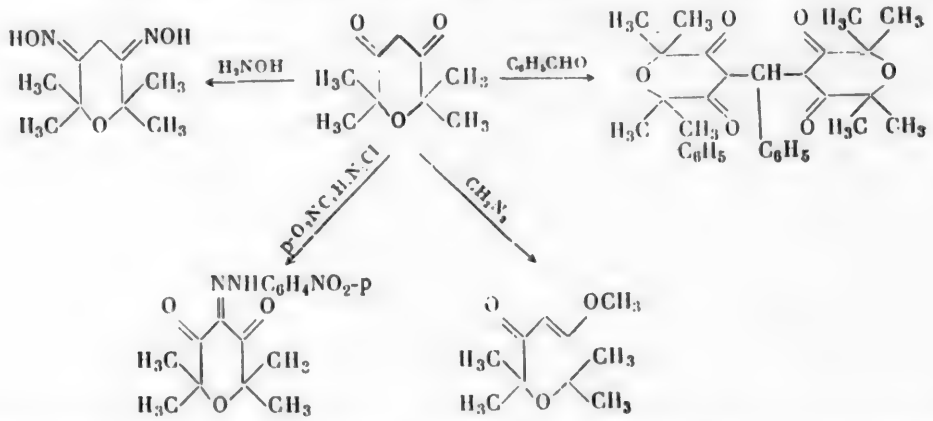


Yields of 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones (calculated on the original α-diketone) can sometimes be considerably increased by subjection to hydrolysis of the crude product obtained by the action of diazomethane on furanidine-3,4-diones.

Like other cyclic β-diketones, 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones do not form copper salts and do not give a coloration with ferric chloride in absolute methanol; however, they dissolve in alkalies or form insoluble sodium salts, while in aqueous methanolic solution they give a faint yellow color with ferric chloride.

The ultraviolet absorption spectra of methanolic solutions of 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones and of the methyl ethers of their enolic forms contain a strong maximum in the 250 mμ region due to the presence of the conjugated system $-\overset{\overset{O}{\|}}{C}-CH=\overset{|}{C}-OCH_3(H)$. The close similarity between the absorption spectra of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione and the methyl ether of its enolic form indicates that 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones are strongly enolized in methanolic solutions and that an intramolecular hydrogen bond is absent. We may therefore conclude that 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones possess the trans-enol structure characteristic of cyclic β-diketones. The ultraviolet absorption spectra of 2,2,6,6-tetramethyltetrahydropyran-3,5-diones in 0.01 N methanolic sodium hydroxide solution exhibit a maximum in the 280 mμ region; this shift in the position of the maximum is characteristic of the transition from the undissociated enolic form to the enolate anion; also the similarity between the absorption coefficients in neutral and alkaline methanol (log ε 4.60 and 4.61, respectively) indicates that enolization is nearly 100% in neutral methanol.*

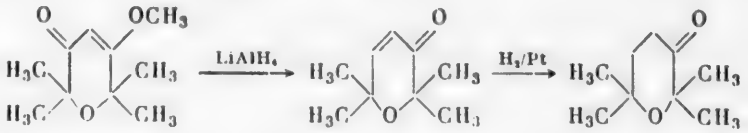
We confirmed the structure of 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones and of the methyl ethers of their enolic forms by means of data for the tetramethyl compound. The preparation of the dioxime and semibenzylidene derivative, azo-coupling with p-nitrophenyldiazonium chloride, and methylation with diazomethane, as well as the spectral data, conclusively point to the presence of a β-dicarbonyl grouping in the ring.



The character of the ring was established by reduction of the methyl ether of the enolic form of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione by lithium aluminum hydride to Δ^4 2,2,6,6-tetramethyldihydro-3-pyrone.

*Determination of the enol content by Meyer's method [24] gave a value for 2,2,6,6-tetramethyltetrahydropyran-3,5-dione that was very much too high (182% of enol). This is typical of 1,3-cyclanediones [25].

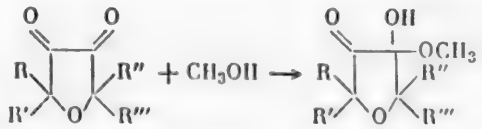
Hydrogenation of this unsaturated ketone in presence of platinum gave 2,2,6,6-tetramethyltetrahydro-3-pyrone, identical with the compound that we prepared earlier [26].



In all cases, excepting 2,2,5,5-tetramethylfuranidine-3,4-dione, good yields of methyl ethers of enolic forms of 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones are obtained only if 10% of methanol (calculated on the volume of reaction mixture) is added. In the absence of methanol the yield of methyl ethers is significant (for example 2,5-dimethyl-2,5-diethylfuranidine-3,4-dione gave only 11% of methyl ether of the corresponding enol of tetrahydropyran-3,5-dione).

The catalytic effect of hydroxyl-containing compounds in the reaction of α-dicarbonyl compounds with diazomethane has already been reported [1, 8]. Expansion of camphorquinone, moreover, by diazomethane was also effected in presence of methanol [21]; it has also been shown that alloxan reacts with diazomethane only in its hydrate form [1]. No data exist, however, for the role of hydroxyl-containing compounds in the ring expansion of α-diketones by diazomethane.

We suggest that since 2,2,5,5-tetraalkylfuranidine-3,4-diones in methanolic solutions exist in the hemiketal form [27], only this form of furanidine-3,4-diones is capable of reacting with diazomethane with ring expansion.



The high yield of methyl ether of the enol form of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione even in the absence of methanol is due to the extreme hygroscopicity of the starting substance [28] so that it always contains a small quantity of the hydrated form whose structure is similar to that of the hemiketal form. During its reaction with diazomethane, water is released and this is apparently sufficient to enable the whole of the diketone to react in the hydrate form. Addition of methanol is therefore not obligatory for preparation of the methyl ether of the enol form of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione, but is desirable since it facilitates the isolation of the end product.

In this connection we may note the extremely interesting fact that ring expansion of triketohexahydroindan by diazomethane goes satisfactorily only in the total absence of water and alcohol [20]; in their presence the triketone reacts with diazomethane in its hydrate form to form other reaction products, apparently with an unchanged number of links in the ring.

EXPERIMENTAL

Sublimation was effected in vacuo (2-3 mm). 2,2,5,5-Tetraalkylfuranidine-3,4-diones were prepared by oxidation of the corresponding 2,2,5,5-tetraalkyl-3-furanidones [28-30]. An ethereal solution of diazomethane was prepared by decomposition of N-nitroso-N-methylurea [31]; titration with benzoic acid showed that 100 ml of solution contained ~ 2.4 g of diazomethane.

Methyl ethers of 2,2,6,6-tetraalkyldihydro-3-pyrone-5-ols. To 300 ml of ethereal solution of diazomethane at 0° was added 30 ml of absolute methanol, followed after 10-15 min (with stirring) by a solution of 0.05 mole of 2,2,5,5-tetraalkylfuranidine-3,4-dione in 50 ml of absolute ether and 10 ml of absolute methanol. The mixture was then heated to 18-20° and allowed to stand overnight. The solvent was taken off in vacuo at room temperature, the yellow semisolid residue or oil (crude methyl ether) dissolved in ligroine, and the precipitate collected after cooling to −70°. The ethers are colorless, crystalline substances, volatile in vacuo, readily soluble in organic solvents (Table 1).

TABLE 1

Constants and Yields of Methyl Ethers of 2,2,6,6-Tetraalkyldihydro-3-pyrone-5-ols

Methyl ethers of 2,2,6,6-tetraalkyl-dihydro-3-pyrone-5-ols	Yield (%)	Sublimation temperature	Melting point after sublimation
2,2,6,6-Tetramethyl	46	65—70°	74—75° •
2,6-Dimethyl-2,6-diethyl	41	70—80	69.8—71.3
2,2,6,6-Bistetramethylene-	18.5 •••	100	46—47
2,2,6,6-Bispentamethylene-	51.5	120—125	124.5—126

•Repeated crystallizations and fractional sublimation are necessary due to the ease of hydrolysis;
•• $\nu_{C=O}$ 1614-1630 cm^{-1}.
••• Low yield owing to the difficulty of separation from the reaction mixture resulting

TABLE 2

Conditions of Preparation, Constants, and Yields of 2,2,6,6-Tetraalkyltetrahydropyran-3,5-

2,2,6,6-Tetraalkyltetrahydro-pyran-3,5-diones and their dioximes	Period of hydrolysis (hr)	Yield (%) of pure ether		Yield (%) of crude ether	Solvent for crystallization •	Sublimation temperature
		calc. on the ether	calc. on the α-diketone			
2,2,6,6-Tetramethyl-	1	92.5	42.5	66 ••	A	100°
Dioxime	—	—	—	—	—	—
2,6-Dimethyl-2,6-diethyl-	1.5	90	37	44	B	140—145
Dioxime	—	—	—	—	—	—
2,2-Dimethyl-6,6-tetramethylene-	2	—	—	40	B	108
Dioxime	—	—	—	—	—	—
2,2,6,6-Bistetramethylene-	1	96.5	18	38	A	120—125
Dioxime	—	—	—	—	—	—
2,2-Dimethyl-6,6-pentamethylene-	2	—	—	41	A	120—130
Dioxime	—	—	—	—	—	—
2,2,6,6-Bispentamethylene-	7 ••••	96	49.5	55	C	—
Dioxime	—	—	—	—	—	—

•Solvents: A) mixture of ligroine and benzene; B) isooctane; C) cyclohexane.
•• Yield referred to diketone with m.p. 151-153.5°.
••• $\lambda_{max}^{CH_3OH}$ 252 mμ, log ε 4.60; $\nu_{C=O}$ 1616 cm^{-1}.
•••• On hydrolysis for 2 hr with a 3 : 2 mixture of 19% hydrochloric acid and dioxane, yield 98%

$\lambda_{max}^{CH_3OH}$ (in mμ)	log ε	Found %		Empirical formula	Calculated %	
		C	H		C	H
248**	4.326	65.26, 65.20	8.79, 8.93	$C_{10}H_{16}O_3$	65.19	8.75
250	4.146	67.67, 67.73	9.50, 9.55	$C_{12}H_{20}O_3$	67.81	9.50
251, 298	4.61, 2.18	71.15, 71.20	8.65, 8.51	$C_{14}H_{20}O_3$	71.16	8.53
252	4.602	72.48, 72.61	9.24, 9.26	$C_{16}H_{24}O_3$	72.69	9.15

otherwise traces of the corresponding diketone are present.

from the low melting point.

diones by Hydrolysis of the Methyl Ethers of Their Enols

Melting point after sublimation	λ_{max} of 0.01 N NaOH in CH_3OH mμ	log ε	Found %			Empirical formula	Calculated %		
			C	H	N		C	H	N
158–158.5°	278***	4.61	63.31, 63.51; CO: 32.74, 32.92	8.42, 8.54	—	$C_5H_{14}O_3$	63.51, CO: 32.91	8.29	—
160–161 (decomp.)	—	—	54.02, 54.14	8.00, 8.19	14.08, 13.86	$C_9H_{16}O_3N_2$	53.98	8.06	13.99
150.8–151.3	277	4.69	66.52, 66.39	9.09, 8.99	—	$C_{11}H_{18}O_3$	66.64	9.15	—
117.5–118	—	—	—	—	12.19, 12.23	$C_{11}H_{20}O_3N_2$	—	—	12.27
152.5–153.5	280	4.89	67.41, 67.57	8.34, 8.33	—	$C_{11}H_{16}O_3$	67.32	8.22	—
143–143.5	—	—	58.46, 58.59	7.99, 8.15	12.52, 12.33	$C_{11}H_{18}O_3N_2$	58.39	8.02	12.38
169–170	282	4.48	70.32, 70.17	8.17, 8.23	—	$C_{13}H_{18}O_3$	70.24	8.16	—
200 (decomp.)	—	—	—	—	10.85, 10.86	$C_{13}H_{20}O_3N_2$	—	—	11.10
161.5–162	275	5.00	68.85, 68.90	8.79, 8.69	—	$C_{12}H_{18}O_3$	68.54	8.63	—
153–154.5	—	—	59.94, 59.71	8.49, 8.54	11.25, 11.34	$C_{12}H_{20}O_3N_2$	59.98	8.39	11.66
193	280	4.60	72.09, 72.07	8.87, 8.93	—	$C_{15}H_{22}O_3$	71.97	8.86	—
217 (decomp.)	—	—	64.08	8.71	10.02, 9.96	$C_{15}H_{24}O_3N_2$	64.26	8.63	9.99

Oxime of methyl ether of 2,2,6,6-tetramethyldihydro-3-pyrone-5-ol. Forms colorless crystals with m.p. 116.5° (from aqueous alcohol and after sublimation at 80-90°).

Found %: N 7.36, 7.46. $C_{10}H_{17}O_3N$. Calculated %: N 7.03.

2,2,6,6-Tetraalkyltetrahydropyran-3,5-diones. a) A suspension of 1 g of pure methyl ether of 2,2,6,6-tetraalkyldihydro-3-pyrone-5-ol in 5 ml of 19% hydrochloric acid* was heated with frequent shaking on a water bath. The diketone was separated after cooling.

b) A mixture of crude methyl ether of 2,2,6,6-tetraalkyldihydro-3-pyrone-5-ol (from 0.05 mole of 2,2,5,5-tetraalkylfuranidine-3,4-dione and 300 ml of ethereal solution of diazomethane) was heated with 50 ml of 19% hydrochloric acid* with stirring on a water bath. The diketone was separated after cooling and washed with ether. In the case of the two lowest homologs the reaction product was extracted with ether, and the extract treated with aqueous alkali. The alkali extract was washed with ether and the diketone brought down with acid.

2,2,6,6-Tetraalkyltetrahydropyran-3,4-diones are colorless, crystalline substances that sublime in vacuo (Table 2).

Dioximes. A solution of 1 mmole of diketone and 4 moles of hydroxylamine in 4 ml of anhydrous pyridine was allowed to stand overnight, heated for 2 hr on a water bath, and poured into water. The dioxime crystallizes from aqueous alcohol (Table 2).

Methylation of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione. To 10 ml of ethereal solution of diazomethane, cooled to 0° and diluted with 20 ml of ether, was added 340 mg of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione in small portions. After termination of the violent reaction, the ether was evaporated in vacuo to leave 360 mg of ether with m.p. 74.5-75° (after sublimation at 60-70°). A mixture with the preparation described above did not have a depressed melting point.

Found %: C 64.96, 65.10; H 8.77, 8.64. $C_{10}H_{16}O_3$. Calculated %: C 65.19; H 8.75.

Methylation of 2,6-dimethyl-2,6-diethyltetrahydropyran-3,5-dione. Treatment of 194 mg of diketone with 10 ml of ethereal solution of diazomethane gave 207 mg of ether with m.p. 69.5-70.5° (after sublimation at 70-80°). No depression of melting point in admixture with the preparation described above.

Phenyldi-(2,2,6,6-tetramethyltetrahydropyran-3,5-dione-4-yl)-methane. A mixture of 340 mg of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione, 212 mg of benzaldehyde, 2 ml of anhydrous pyridine, and one drop of piperidine was heated for 2 hr on a water bath, the pyridine taken off in vacuo, and the residue crystallized from a mixture of ligroine and benzene. Yield 390 mg (91%) with m.p. 123-125° (after reprecipitation from alkali solution and crystallization from aqueous methanol); colorless needles.

Found %: C 70.11, 70.25; H 7.53, 7.72. $C_{25}H_{32}O_6$. Calculated %: C 70.05; H 7.53.

4-p-Nitrophenylhydrazone of 2,2,6,6-tetramethyltetrahydropyran-3,4,5-trione. A solution (cooled to 0°) of p-nitrophenyldiazonium chloride (from 280 mg of p-nitroaniline in 9.5 ml of 0.7 N hydrochloric acid) was added with stirring to a solution of 340 mg of 2,2,6,6-tetramethyltetrahydropyran-3,5-dione in 5 ml of 1.15 N sodium hydroxide. After 15 min, the precipitate was separated and washed with dilute hydrochloric acid. Yield 580 mg (90.5%) with m.p. 181-182° (from aqueous alcohol); bright-yellow needles.

Found %: C 56.56, 56.51; H 5.59, 5.61; N 13.27, 13.43. $C_{15}H_{17}O_5N_3$. Calculated %: C 56.42; H 5.37; N 13.16.

Δ^4-2,2,6,6-Tetramethyldihydro-3-pyrone. To a solution of lithium aluminum hydride (from 0.96 g of lithium hydride and 8.0 g of aluminum bromide in 150 ml of absolute ether) was added a solution of 5.52 g of the methyl ether of 2,2,6,6-tetramethyldihydro-3-pyrone-5-ol in 50 ml of absolute ether. The stirred mixture was boiled for 1.5 hr. After 12 hr stirring and cooling to 0°, 20 ml of water was added, the mixture was cooled to −6°, and in the course of 1.5 hr 20 ml of concentrated sulfuric acid was added. The mixture was then held for 1.5 hr at −5° and for 1 hr at 8-12°. The precipitate was separated and washed with ether; the ethereal layer was collected and the aqueous layer extracted with ether. The combined ethereal extracts were washed with

*Acid of 10% concentration was used with the methyl ether of 2,2,6,6-tetramethyldihydro-3-pyrone-5-ol.

saturated sodium carbonate solution, then with water, and dried with magnesium sulfate. After distillation of the ether, the residue was fractionated in vacuo to give 3.89 g (84%) of yellowish oil with a camphor-like odor.

B.p. 79-80° (19 mm), 74-75° (17 mm), $n^{20}D$ 1.4600, d^{20}_4 0.9731, MR_D 42.41. $C_{19}H_{14}O_2F$. Calculated 42.75; $\lambda_{max}^{CH_3OH}$ 338 mμ, log ε 1.794, $\nu_{C=O}$ 1672-1694 cm^{-1}.

Found %: C 70.16, 70.06; H 9.38, 9.28. $C_9H_{14}O_2$. Calculated %: C 70.10; H 9.15.

Semicarbazone: m.p. 178.3-179.3° (from very dilute alcohol), $\lambda_{max}^{CH_3OH}$ 272 mμ, log ε 4.37.

Found %: N 20.22, 20.10. $C_{10}H_{17}O_2N_3$. Calculated %: N 19.89.

The dibromide was prepared by addition of a solution of 320 mg of bromine in 10 ml of anhydrous chloroform to 308 mg of the unsaturated ketone and distillation of the solvent in vacuo (yield 600 mg). The compound was unstable and loses hydrogen bromide during recrystallization, giving Δ⁴-4 (or 5)-bromo-2,2,6,6-tetramethyldihydro-3-pyrone; m.p. 97.3-98° (from ligroine at −70° and after sublimation at 70-80°), $\lambda_{max}^{CH_3OH}$ 252, 332-340 mμ, log ε 3.851, 1.770; colorless needles.

Found %: C 46.51, 46.54; H 5.91, 5.86. $C_9H_{13}O_2Br$. Calculated %: C 46.37; H 5.62.

2,2,6,6-Tetramethyltetrahydro-3-pyrone. A solution of 1.54 g of Δ⁴-2,2,6,6-tetramethyldihydro-3-pyrone in 50 ml of alcohol was hydrogenated (with shaking) in presence of reduced platinum dioxide. After 2 hr the hydrogen absorption was 235 ml (NTP) (calculated 224 ml). Distillation gave 1.25 g (80%) of colorless liquid with a camphor-like odor; b.p. 75-77° (20 mm), $n^{20}D$ 1.4410; literature data [26]: b.p. 62-63° (9 mm), $n^{20}D$ 1.4413.

Semicarbazone: m.p. 196-198° (from very dilute alcohol); no depression of melting point in admixture with an authentic specimen [26].

We extend out heartfelt thanks to Yu. K. Yur'ev for his unremitting interest in our work.

SUMMARY

1. Diazomethane acts on 2,2,5,5-tetraalkylfuranidine-3,4-diones with ring expansion and formation of methyl ethers of the enolic forms of 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones.

2. The synthesis of methyl ethers of the enolic forms of 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones and their subsequent hydrolysis can serve as a preparative route to 2,2,6,6-tetraalkyltetrahydropyran-3,5-diones.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

SYNTHESIS OF 2,5-SUBSTITUTED 1,3,4-THIADIAZOLES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4024-4026, December, 1960
Original article submitted January 25, 1960

During an investigation of the physiological activity of thiazoles we required some 2,5-substituted 1,3,4-thiadiazoles for testing. Only a few of these are described in the literature, evidently due to the difficulty of preparing them. The synthesis is based essentially on heating of N,N'-diacylhydrazines with P_2S_5 at 200° in vacuo [1].

We developed a more convenient method of preparation of 2,5-substituted thiadiazoles which makes these compounds (with identical or different radicals in the 2 and 5 positions) very easily accessible.

The method consists in reaction of thiohydrazides with acid chlorides in pyridine solution in accordance with the equation

Intermediate products in this reaction are evidently acyl derivatives of thiohydrazides which do not come down under the reaction conditions and quickly cyclize to thiadiazole. Several 2,5-substituted 1,3,4-thiadiazoles described in the literature were prepared by this method, as well as new representatives of the class containing aliphatic, aromatic, and heterocyclic radicals.

By replacing chlorides of monobasic acids by anhydrides or chlorides of dibasic acids, it is possible to obtain thiadiazoles with a carboxyl group in the side chain, and also bisthiadiazoles.

The products are colorless or faint yellow substances, crystallizing with facility from alcohol. Nearly all the thiadiazoles fluoresce strongly in the near ultraviolet, both in the crystalline state (see table) and in solution. Compounds containing naphthyl and pyridine residues have a yellow fluorescence in an acid medium, and a bright-blue color at pH 9-10. Compounds containing nitrophenyl and $C_{17}H_{35}$ groups do not fluoresce.

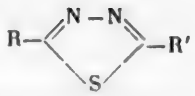
The properties of the prepared thiadiazoles are set forth in the table.

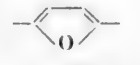
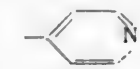
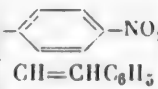
EXPERIMENTAL

The benzoic acid thiohydrazide required for the work was prepared by Holmberg's method and had m.p. 78-79°. The literature [3] gives m.p. 81-82°. The thiohydrazide of α-naphthalenecarboxylic acid, not described in the literature, was prepared by a similar route.

Thiohydrazide of α-naphthalenecarboxylic acid. α-Naphthylmagnesium bromide, prepared from 2.5 g of magnesium, 20 g of α-bromonaphthalene, and 50 ml of absolute ether, was gradually added to a cooled solution of 6.6 ml of carbon disulfide in 30 ml of ether. The mixture was left to stand for 10-12 hr. Finely crushed ice was then carefully added (with cooling). The solution was filtered and the lower aqueous layer collected. Into the aqueous solution of the dithio acid was run a solution of 12.5 g of monochloroacetic acid and 17 g of sodium

2,5-Substituted 1,3,4-Thiadiazoles



R	R′	Empirical formula	Yield (%)	Melting point	Fluorescence of crystals	% N found	% N calc.
C_6H_5	CH_3	$C_9H_8N_2S$	62	109—110° 107 [2]	Bright yellow	—	—
C_6H_5	$C_{17}H_{35}$	$C_{25}H_{40}N_2S$	40	78—79	Does not fluoresce	7.07	7.00*
C_6H_5	C_6H_5	$C_{14}H_{10}N_2S$	74	141—142, 141—142 [1]	Intense violet	—	—
C_6H_5	$CH{=}CHC_6H_5$	$C_{16}H_{12}N_2S$	90	136—138, 137 [2]	Intense blue-violet	—	—
C_6H_5		$C_{12}H_8ON_2S$	87	108—109	Intense violet	12.41	12.20
C_6H_5		$C_{13}H_9N_3S$	62	181—183	Violet	17.08	17.50**
α-$C_{10}H_7$	C_6H_5	$C_{18}H_{12}N_2S$	50	112—113	Intense blue-violet	9.50	9.72***
α-$C_{10}H_7$		$C_{18}H_{11}O_2N_3S$	71	209—211	Does not fluoresce	12.39	12.61
α-$C_{10}H_7$	$CH{=}CHC_6H_5$	$C_{20}H_{14}N_2S$	87	97—98	Bright blue	8.87	8.97
α-$C_{10}H_7$		$C_{17}H_{11}N_3S$	93	139—140	Bright blue	14.29	14.51

*Found %: S 8.13, 7.95. Calculated %: S 8.00.

**Found %: S 13.34, 13.58. Calculated %: S 13.38.

***Found %: S 11.02, 10.84. Calculated %: S 11.11.

carbonate in 45 ml of water. The mixture was allowed to stand for 10-12 hr, and carefully acidified with a solution of 8 ml of conc. H_2SO_4 in 25 ml of water. Thionaphthoylthioglycolic acid separated as a red oil. It was separated from the aqueous layer and (without purification) dissolved in 30 ml of 1 N alkali; the solution was filtered and 5 ml of hydrazine hydrate added. The mixture was heated on a water bath. The thiohydrazide came out as an oil. After cooling, acetic acid was added until separation was complete. The cooled solution was decanted from the oil, the oil was dissolved in alcohol, and the solution filtered in presence of carbon and evaporated to dryness. The residue was crystallized from benzene or from a large volume of water. Yield 2.8 g, m.p. 96-98°.

Found %: N 13.94. $C_{11}H_{10}N_2S$. Calculated %: N 13.86.

2,5-Substituted 1,3,4-thiadiazoles. Excess of acid chloride was added gradually to anhydrous pyridine. The thiohydrazide of the acid was then added with cooling. The mixture was boiled for 30 min. After cooling, the mass was poured into water, and the precipitate was filtered and washed with water. If necessary, the mixture was left to stand for a few hours for separation of the precipitate. The dry thiadiazole was crystallized from dilute alcohol. Under the microscope the prepared thiadiazoles have the form of lustrous plates or prisms.

SUMMARY

A convenient method is proposed for preparation of 2,5-substituted 1,3,4-thiadiazoles, consisting in reaction of thiohydrazides with acid chlorides.

This method was employed for preparation of ten thiadiazoles, seven of which have not been described in the literature.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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p-TRIFLUOROMETHYLPHENYLTETRAFLUOROPHOSPHORANE AND ITS DERIVATIVES

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Translated from Zhurnal Obshchei Khimii Vol. 30, No. 12, pp. 4026-4030, December, 1960
Original article submitted January 23, 1960

In the preceding publications we described some aryltetrafluorophosphoranes, arylphosphonic difluorides, and arylthiophosphinic acids, their properties, and their transformations [1, 2].

Continuing our studies in this field, we decided to synthesize a phenyltetrafluorophosphorane substituted by the electronegative trifluoromethyl group and to establish whether this compound was more resistant to hydrolysis. With this objective we prepared p-tolyldichlorophosphine, chlorinated the latter in the cold to p-tolyltetrachlorophosphorane, and effected further chlorination in the methyl group by heating in presence of azodiisobutyronitrile. However, the chlorination did not go smoothly. Heating at above 140° led to cleavage of the compound with formation of phosphorus pentachloride, p-chlorobenzotrichloride, and a small quantity of p-chlorobenzylidene chloride. At a temperature below 130° the chlorination could not easily be completed. After a number of experiments we were able to establish the conditions for preparation of a substance whose chlorine content indicated the structure of p-trichloromethylphenyltetrachlorophosphorane. This compound was extremely hygroscopic and not easily amenable to purification. It was therefore converted by treatment with sulfur dioxide into p-trichloromethylphenylphosphonic dichloride which was purified by distillation in vacuo. Its dianilide was prepared.

Fluorination of technical p-trichloromethylphenyltetrachlorophosphorane and of p-trichloromethylphenylphosphonic dichloride with antimony trifluoride or zinc fluoride was accompanied by a violent reaction, and a difficultly separable mixture of substances was obtained that fumed in the air and had a serious corrosive action on glass. We failed to isolate individual substances.

Also unsuccessful was an attempt to chlorinate benzyltetrachlorophosphorane to α,α-dichlorobenzyltetrachlorophosphorane. Benzyldichlorophosphine was chlorinated in presence of azodiisobutyronitrile in the course of an hour at 85-90°, and also in carbon tetrachloride solution with boiling for two days, or with phosphorus pentachloride at 60-85°. After passage of a stream of sulfur dioxide, the reaction products were fractionated. Mixtures of benzyl chloride, benzylidene chloride and, apparently, benzyl- and α-chlorobenzylphosphonic dichlorides were obtained in all cases. In special experiments it was established that benzyltetrachlorophosphorane starts to decompose at the low temperature of 80° with formation of benzyl chloride and phosphorus trichloride. α-Chloro derivatives of benzyltetrachlorophosphorane apparently decompose with even greater facility.

After unsuccessful attempts to chlorinate and fluorinate p-tolyldichlorophosphine, we decided to prepare p-trifluoromethylphenyltetrafluorophosphorane from a compound already containing the trifluoromethyl group. The selected starting substance was p-bromobenzotrifluoride which was converted with phosphorus trichloride, via the organomagnesium and then the organozinc compound, into p-trifluoromethylphenyldichlorophosphine. The latter was chlorinated and then fluorinated with the help of antimony trifluoride to give p-trifluoromethylphenyltetrafluorophosphorane.

$$p\text{-}CF_3C_6H_4Br \xrightarrow[ZnCl_2]{Mg} p\text{-}CF_3C_6H_4ZnBr \xrightarrow{PCl_3} p\text{-}CF_3C_6H_4PCl_2 \xrightarrow{Cl_2}$$

$$\longrightarrow p\text{-}CF_3C_6H_4PCl_4 \xrightarrow{SbF_3} p\text{-}CF_3C_6H_4PF_4.$$

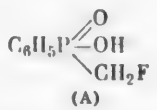
p-Trifluoromethylphenyltetrafluorophosphorane is a colorless liquid, fuming in the air, corrosive to glass, soluble in all organic solvents. Reaction with aniline without exclusion of atmospheric moisture gives the anilide of p-trifluoromethylphenylmonofluorophosphonic acid.

Treatment of p-trifluoromethylphenyltetrachlorophosphorane with sulfur dioxide leads to p-trifluoromethylphenylphosphonic dichloride, hydrolysis of which gives the phosphonic acid, while treatment with aniline gives the dianilide of the acid. The dichloride is converted by zinc fluoride into p-trifluoromethylphenylphosphonic difluoride. The latter reacts with isopropyl alcohol in presence of triethylamine to give the isopropyl ester of p-trifluoromethylphenylmonofluorophosphonic acid. p-Trifluoromethylphenyldichlorophosphine reacts with sulfur in presence of aluminum chloride to give p-trifluoromethylphenylthiophosphonic dichloride.

In addition to carrying out the foregoing syntheses, we continued our study of the chemical properties of phenyltetrafluorophosphorane. In one of the preceding papers [3] it was shown that phenyltetrachlorophosphorane reacts with diazomethane in such a manner that two methylene groups enter the molecule:

$$C_6H_5PCl_4 + 2CH_2N_2 \longrightarrow C_6H_5PCl_2(CH_2Cl)_2.$$

Phenyltetrafluorophosphorane reacts very much less energetically with diazomethane. After hydrolysis of the reaction product, we were able to isolate a substance whose properties and analysis corresponded to phenyl-ω-fluoromethylphosphonic acid, a solid, crystalline substance (A) giving an acid reaction to Congo. Analysis of the ammonium salt of this acid also confirmed its composition.



(A)

It has been declared in the literature [4] that attempts to synthesize fluorides of carboxylic acids directly from the acids and the fluorides or oxyfluorides of nonmetals are doomed to failure or inexpedient. Our very first experiments demonstrated the incorrectness of this assertion. Reaction of phenyltetrafluorophosphorane with propionic acid gives propionyl fluoride. However, the corrosion of glass by the hydrogen fluoride evolved is an obstacle to the performance of this reaction in a glass apparatus. Corrosion of glass does not occur if a salt of propionic acid (such as the lithium salt) is taken.

EXPERIMENTAL

p-Trichloromethylphenylphosphonic dichloride. Chlorination of 23.7 g of p-tolyldichlorophosphine was carried out for 21 hr in a reaction vessel equipped with thermometer, chlorine inlet tube, and calcium chloride tube, the temperature being gradually raised from 80 to 130°. Azodiisobutyronitrile was used as a catalyst in some runs. Sulfur dioxide gas was then passed through with cooling. After vacuum distillation the yield of dichloride was 28.6 g (75%).

B.p. 129-131° (0.05 mm), $n^{21}D$ 1.5830, d^{21}_{20} 1.5907.

Found %: P 9.97, 10.22. $C_7H_4OPCl_5$. Calculated %: P 9.93.

Dianilide of p-trichloromethylphenylphosphonic acid. p-Trichloromethylphenylphosphonic dichloride was mixed with four moles of aniline in benzene. After aniline hydrochloride had been washed out with water, the dianilide was recrystallized from methanol. Needles with m.p. 194-195°.

Found %: Cl 24.53, 24.66; N 6.70, 6.75. $C_{19}H_{16}ON_2PCl_3$. Calculated %: Cl 25.04; N 6.58.

Benzyldichlorophosphine. Prepared from benzyl bromide, via benzylzinc bromide, and phosphorus trichloride [5].

p-Bromobenzotrifluoride. Prepared by fluorination of p-bromobenzotribromide [6].

p-Trifluoromethylphenyldichlorophosphine. The procedure for synthesis was similar to that for the phenyldichlorophosphine [7]. From 48.1 g of p-bromobenzotrifluoride was obtained 15.9 g (33.1%) of p-trifluoromethylphenyldichlorophosphine with b.p. 92-93° (14 mm).

Found %: P 12.28, 12.35. $C_7H_4PF_3Cl_2$. Calculated %: P 12.59.

p-Trifluoromethylphenyltetrafluorophosphorane was prepared similarly to phenyltetrafluorophosphorane [1]. p-Trifluoromethylphenyltetrachlorophosphorane (9 g) was mixed with antimony trifluoride (7.5 g). The reaction was violent. Yield 3.8 g (53.6%); b.p. 140-141°, d^{21}_{20} 1.5584.

Found %: P 12.24; 12.46. $C_7H_4PF_7$. Calculated %: P 12.30.

p-Trifluoromethylphenylmonofluorophosphonic acid anilide. Aniline and p-trifluoromethylphenyltetrafluorophosphorane were mixed in 2:1 molar ratio without exclusion of atmospheric moisture. M.p. 173-174° after crystallization from dichloroethane.

Found %: N 4.69, 4.81. $C_{13}H_{12}O_2NPF_4$. Calculated %: N 4.36

p-Trifluoromethylphenylphosphonic dichloride. p-Trifluoromethylphenyldichlorophosphine (6.4 g) was chlorinated to the tetrachloro derivative, which was then treated with sulfur dioxide. Yield of dichloride 6.08 g (88.8%), $n^{23}D$ 1.4940. d^{23}_{20} 1.5286.

Found %: P 12.00, 12.22. $C_7H_4OPF_3Cl_2$. Calculated %: P 11.79.

p-Trifluoromethylphenylphosphonic acid dianilide. Benzene solutions of aniline and the dichloride of the acid were mixed. The product crystallized from aqueous alcohol; m.p. 193-194°.

Found %: N 7.44, 7.56; P 8.20, 7.91. Calculated %: N 7.45; P 8.24. $C_{19}H_{16}ON_2PF_3$.

p-Trifluoromethylphenylphosphonic acid was obtained by hydrolysis of the dichloride. M.p. 177-179° after crystallization from water and then from a mixture of benzene and ether. Readily soluble in ether, acetone, insoluble in benzene, chloroform, and ligroine.

Found %: P 13.61, 14.00. $C_7H_6O_3PF_3$. Calculated %: P 13.72.

p-Trifluoromethylphenylthiophosphonic dichloride. Prepared by addition of sulfur to the dichlorophosphine in presence of aluminum chloride. Yield 88.8%; b.p. 89-90° (3 mm), $n^{21}D$ 1.5445, d^{21}_{20} 1.5254.

Found %: P 11.00, 10.94. $C_7H_4SPF_3Cl_2$. Calculated %: P 11.11.

p-Trifluoromethylphenylphosphonic difluoride. From 6.1 g of p-trifluoromethylphosphonic difluoride From 6.1 g of p-trifluoromethylphosphonic dichloride and 2.9 g of zinc fluoride was obtained 4.7 g (88.1%) of the difluoride; b.p. 186-187°.

Found %: P 13.21, 13.60. $C_7H_4POF_5$. Calculated %: P 13.48.

Isopropyl ester of p-trifluoromethylphenylmonofluorophosphonic acid. A solution of 1 ml of isopropyl alcohol and 1.5 ml of triethylamine in 25 ml of benzene was stirred into a solution of 2.5 g of the difluoride in 25 ml of benzene. The mixture was left overnight and then washed with water. The benzene solution was dried, the benzene distilled off, and the product distilled in vacuo. Yield 1.7 g (58.2%).

B.p. 94-95° (8 mm), $n^{25}D$ 1.4333, d^{20}_{25} 1.2853.

Found %: P 11.21, 11.25. $C_{10}H_{11}O_2PF_4$. Calculated %: P 11.48.

Phenyl-ω-fluoromethylphosphonic acid. A solution of 6.7 g of phenyltetrafluorophosphorane in 100 ml of absolute ether was placed in a reactor equipped with dropping funnel, thermometer, and stirrer. A solution of 3 g of diazomethane in 150 ml of absolute ether was added at −20 to −30°, and the mixture was left overnight. After the ether had been taken off, the oily product was treated with water. The deposited crystals were filtered. M.p. 94-95° (from a mixture of benzene and ligroine). Yield 2 g (31.7%). Readily soluble in alcohol, water, and benzene, sparingly in ligroine.

Found %: F 11.17, 10.92. Equiv. 1.01, 1.02. $C_7H_8O_2PF$. Calculated %: F 10.92. Equiv. 1.0.

Ammonium salt. Prepared by evaporation of a mixture of aqueous ammonia and phenyl-ω-fluoromethylphosphonic acid.

Found %: N 7.35, 7.38. $C_7H_7O_2PF \cdot NH_4$. Calculated %: N 7.33.

Reaction of phenyltetrafluorophosphorane with propionic acid. A mixture of 19.5 g of phenyltetrafluorophosphorane and 8 ml of propionic acid was placed in a flask with a Wurtz fitting and a condenser (the whole

set-up was constructed of copper with ground-glass connections). The mixture was heated with a burner. A liquid (6.8 g) was distilled off. After redistillation the yield of fluoride with b.p. 44-45° was 4.2 g (52%). The anilide with m.p. 104-105° was prepared.

Reaction of phenyltetrafluorophosphorane with lithium propionate. Dry lithium salt (3.8 g) was added to 9.7 g of the phosphorane in a Wurtz flask gently heated with a burner. A liquid with b.p. 42-48° came over. After redistillation the yield of propionyl fluoride with b.p. 44-45° was 1.5 g (41.8%).

SUMMARY

p-Trifluoromethylphenyldichlorophosphine, p-trifluoromethylphenyltetrafluorophosphorane, p-trifluoromethylphenylphosphonic difluoride, and some of their derivatives were prepared.

Hydrolysis of the product of reaction of phenyltetrafluorophosphorane with diazomethane gave phenyl-ω-fluoromethylphosphonic acid.

Starting from propionic acid as the acid component, it was shown that phenyltetrafluorophosphorane reacts with carboxylic acids with formation of fluorides of the carboxylic acids.

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5. Th. Weil, B. Prijs, and H. Erlenmeyer, Helv. Chim. Acta 36, 1314 (1953).
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BROMINATION AND AZO COUPLING REACTIONS IN THE NAPHTHOFURAN AND BENZINDOLE SERIES

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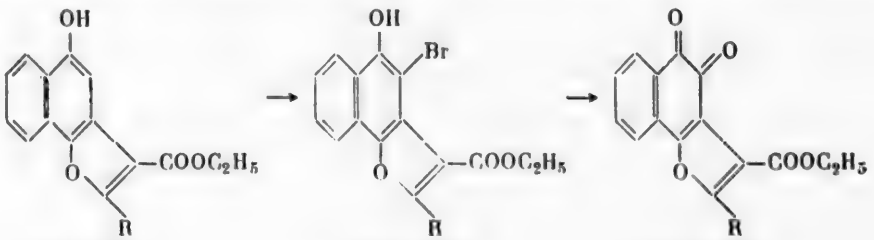
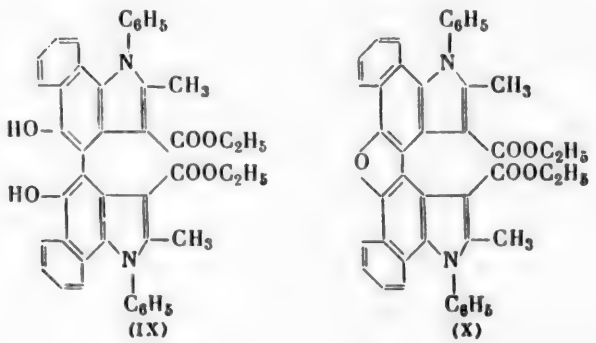
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4030-4034, December, 1960
Original article submitted January 19, 1960

Bromination of hydroxy derivatives of naphthofuran (I), (II) by dioxane dibromide and bromosuccinimide leads to replacement of the hydrogen atom in the 4 position by a bromine atom. Derivatives of 5-hydroxy-4-bromonaphthofuran (III), (IV) are formed. The position of the bromine atom in the products was verified by their oxidation to o-quinones of the naphthofuran series (V), (VI), which were characterized in one of our earlier studies [1].



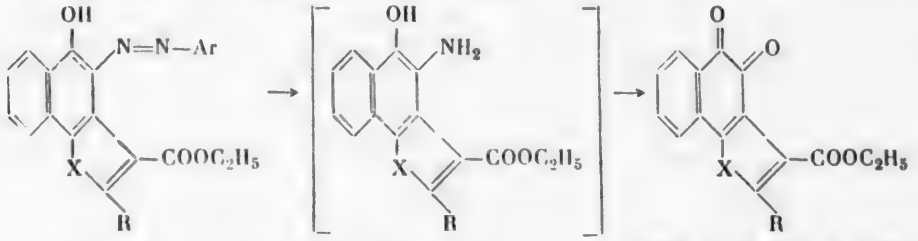
(I) R = CH_3; (II) R = C_6H_5.
(III) R = CH_3; (IV) R = C_6H_5.
(V) R = CH_3; (VI) R = C_6H_5.

Bromination of 1,2-dimethyl-3-carbethoxy-5-hydroxybenzindole (VII) and 1-phenyl-2-methyl-3-carbethoxy-5-hydroxybenzindole (VIII) leads to secondary reactions. Bromination of the N-phenylbenzindole derivative (VIII) with dioxane dibromide gave a bromine-free substance. The analysis and qualitative reactions of this compound indicated the structure of a bisbenzindole (IX). Treatment of (VIII) with bromosuccinimide gave another substance with the proposed structure (X). This differed from (IX) in containing one molecule of water less. Its properties were also different. Bromination of the N-methylbenzindole derivative (VII) leads to formation of resinous polymers.



(IX) (X)

Reaction of derivatives of naphthofuran (I), (II), and of benzindole (VII), (VIII) with diazo compounds in presence of sodium acetate in dioxane gave a series of azo dyes (XI)-(XVIII). The structure of the latter was confirmed by reduction to the aminohydroxy derivatives which were oxidized (without separation from the reaction liquid) to the previously prepared [1] substituted o-quinones (V), (VI), (XIX), (XX).



(XI) X = O, R = CH_3, Ar = -  ;

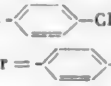
(XII) X = O, R = CH_3, Ar = -  ;

(XIII) X = O, R = C_6H_5, Ar = -  ;

(XIV) X = O, R = C_6H_5, Ar = -  ;

(XV) X = N–CH_3, R = CH_3, Ar = -  ;

(XVI) X = N–CH_3, R = CH_3, Ar = -  ;

(XVII) X = N–C_6H_5, R = CH_3, Ar = - 

(XVIII) X = N–C_6H_5, R = CH_3, Ar = -  .

(XIX) X = N–CH_3, R = CH_3;
(XX) X = N–C_6H_5, R = CH_3.

EXPERIMENTAL

2-Methyl-3-carbethoxy-4-bromo-5-hydroxynaphthofuran (III). a) Bromination with dioxane dibromide. A solution of dioxane dibromide, prepared by dissolving 4 g of bromine in 30 ml of dioxane, was added dropwise to a solution of 6 g of naphthofuran (I) in 60 ml of dioxane. The reaction liquid was left for half an hour at room temperature. After addition of 100 ml of water, the solution was left overnight in a refrigerator. The crystals were collected and recrystallized. Yield 5 g of (III) with m.p. 91-92° (from benzene).

Found %: C 55.10, 55.03; H 3.84, 3.97; Br 22.75, 22.88. $C_{16}H_{13}O_4Br$. Calculated %: C 55.01; H 3.73; Br 22.92.

b) Bromination with bromosuccinimide. To a suspension of 4.05 g of (I) in 15 ml of carbon tetrachloride was added 2.5 g of bromosuccinimide, and the reaction solution boiled for 40 min on a water bath. The resulting precipitate was filtered off. The mother liquor was allowed to evaporate at room temperature, and the deposited crystals recrystallized from benzene. Yield of compound (III) 1.26 g, m.p. 91-91.5°. A mixture with (III) obtained in the preceding experiment had an unchanged melting point.

2-Phenyl-3-carbethoxy-4-bromo-5-hydroxynaphthofuran (IV). a) Bromination with dioxane dibromide. Bromination conditions were as for compound (I). Reaction components were 3 g of (II) and 2 g of bromine in 40 ml of dioxane. Yield of bromide (IV) 1.71 g; m.p. 141-142° (from alcohol).

Found %: C 61.45, 61.33; H 3.59, 3.69. $C_{21}H_{15}O_4Br$. Calculated %: C 61.32; H 3.67.

b) Bromination with bromosuccinimide. Experimental conditions were as for bromination of (I), using 4.4 g of (II) and 2.4 g of bromosuccinimide in 16 ml of carbon tetrachloride. Yield of bromide (IV) 4 g, m.p. 142-142.5° (from benzene). No depression of melting point in admixture with (IV) from the preceding experiment.

Action of dioxane dibromide on 1-phenyl-2-methyl-3-carbethoxy-5-hydroxybenzindole (VIII). A solution of dioxane dibromide in dioxane, prepared from 1.76 g of bromine and 17 ml of dioxane, was added in 10 min at room temperature with good stirring to a suspension of 3.45 g of product (VIII) in 30 ml of dioxane. The reaction mixrure was left for 30 min. The precipitate was filtered, washed with alcohol, and recrystallized

Azo Dyes, Derivatives of Naphthofuran and Benzindole

Azo dyes*	Yield (g), color, quantity of initial hydroxycompound (g)	Melting point	Found, %		Empirical formula	Calc., %	
			C	H		C	H
2-Methyl-3-carbethoxy-4-(p-nitrophenylazo)-5-hydroxynaphthofuran (XI)	2.07, red 1.35	234—234.5°	62.91, 62.63	4.17, 4.28	$C_{22}H_{17}O_6N_3$	63.00	4.09
2-Methyl-3-carbethoxy-4-(p-tolylazo)-5-hydroxynaphthofuran (XII)	3.7, bright-red 2.7	160—162	71.12, 71.45	5.35, 5.28	$C_{23}H_{20}O_4N_2$	71.12	5.19
2-Phenyl-3-carbethoxy-4-(p-nitrophenylazo)-5-hydronaphthofuran (XIII)	2.35, dark-red 1.66	238—238.5	67.59, 67.22	4.14, 4.07	$C_{27}H_{19}O_6N_3$	67.35	3.98
2-Phenyl-3-carbethoxy-4-(p-tolylazo)-5-hydroxynaphthofuran (XIV)	4.4, red 3.32	201—201.5	74.91, 74.85	5.13, 4.94	$C_{28}H_{22}O_4N_2$	74.65	4.92
1,2-Dimethyl-3-carbethoxy-4-(p-nitrophenylazo)-5-hydroxybenzindole (XV)	1.1, dark-red 1.42	180—181	63.74, 63.42	4.47, 4.68	$C_{23}H_{20}O_5N_4$	63.88	4.66
1,2-Dimethyl-3-carbethoxy-4-(p-tolylazo)-5-hydroxybenzindole (XVI)	1.4, dark-red 2.83	200.5—201.5	71.81, 71.94	6.02, 5.85	$C_{24}H_{23}O_3N_3$	71.80	5.78
1-Phenyl-2-methyl-3-carbethoxy-4-(p-nitrophenylazo)-5-hydroxybenzindole (XVII)	1.2, dark-red 1.73	255—256	68.39, 68.08	4.77, 4.70	$C_{28}H_{22}O_5N_4$	68.01	4.58
1-Phenyl-2-methyl-3-carbethoxy-4-(p-tolylazo)-5-hydroxybenzindole (XVIII)	2.78, red 3.45	217—217.5	75.41, 75.27	5.79, 5.46	$C_{29}H_{25}O_3N_3$	75.14	5.44

*Azo coupling in synthesis of dye (XVIII) was performed at 10-12°, and in the remaining experiments at 0-5°.

from toluene. Yield of compound (IX) 2.2 g with m.p. 257-258°. Compound (IX) does not contain bromine; its solution in dioxane acquires a violet color; it gives a positive reaction (red color) with ferric chloride.

Found %: C 76.58, 76.70; H 5.46, 5.44. $C_{44}H_{36}O_6N_2$. Calculated %: C 76.73; H 5.27.

Action of bromosuccinimide on 1-phenyl-2-methyl-3-carbethoxy-5-hydroxybenzindole (VIII). To a suspension of 1 g of (VIII) in 9 ml of glacial acetic acid at room temperature was added 0.45 g of bromosuccinimide. With good stirring the benzindole (VIII) gradually dissolved and the color of the solution changed from yellow to green. At the same time a solid came down, and was filtered and recrystallized from toluene. Yield of (X) 0.52 g, m.p. 325-327°. Compound (X) does not contain bromine and does not give a coloration with ferric chloride.

Found %: C 79.18, 79.20; H 4.86, 5.03. $C_{44}H_{34}O_5N_2$. Calculated %: C 78.79, H 5.11.

Oxidation of 2-methyl-3-carbethoxy-4-bromo-5-hydroxynaphthofuran (III). To a well-stirred suspension of 0.75 g of (III) in 10 ml of glacial acetic acid was added a solution of 0.66 g of chromic oxide in water, and stirring was continued for 20 min at 10-12°. The resulting solution was diluted with water and cooled. The viscous, red mass, containing quinone (V), was separated and dissolved in acetic acid with heating. The resulting solution was heated with 0.5 g of o-phenylenediamine. The yellow precipitate of phenazine derivative was filtered. Yield 0.22 g, m.p. 194° (from alcohol), in agreement with the melting point of the previously prepared phenazine derivative [1].

Oxidation of 2-phenyl-3-carbethoxy-4-bromo-5-hydroxynaphthofuran (IV). To a well-stirred suspension of 0.95 g of bromide (IV) in 11 ml of glacial acetic acid, cooled to 10-12°, was gradually added chromic acid prepared from 0.88 g of chromic oxide and 1 ml of water. The reaction liquid was stirred for an hour and cooled. The red crystals of quinone (VI) were filtered. Yield 0.47 g; m.p. 191-191.5° (from alcohol) corresponding to the melting point of quinone (VI) previously obtained [1].

2-Methyl-3-carbethoxy-4-(p-nitrophenylazo)-5-hydroxynaphthofuran (XI). To a well-stirred suspension of 1.35 g of (I) in 25 ml of dioxane at 4° was gradually added a solution of diazonium salt prepared from 0.9 g of p-nitroaniline, 1.5 ml of concentrated hydrochloric acid, 20 ml of water, 0.5 g of sodium nitrite, and (later) 1.35 g of sodium acetate. The reaction mixture was stirred for 2 hr at 0-5°. The solution was then allowed to stand at 0° for several hours, and the red crystals were filtered and dried. Purification from the chloroform-insoluble starting substance was effected by reprecipitation from chloroform solution with ligroine. Yield 2.07 g, m.p. 234-234.5°.

Found %: C 62.91, 62.63; H 4.17, 4.28. $C_{22}H_{17}O_6N_3$. Calculated %: C 63.00; H 4.09.

Azo dyes (XII)-(XVIII) were prepared similarly (see table).

Conversion of 2-methyl-3-carbethoxy-4-(p-tolylazo)-5-hydroxynaphthofuran (XII) into 2-methyl-3-carbethoxy-4,5-dioxonaphthofuran (V). Zinc dust was added to a boiling solution of 0.4 g of azo compound (XII) in 20 ml of acetic acid until the red solution had lost its color. The solution was filtered from the slurry and chromic acid (prepared by dissolving 0.3 g of chromic acid in water) was added. Oxidation was performed under the conditions described earlier [1]. Orange crystals of o-quinone (V) were obtained, m.p. 140-140.5°.* The phenazine derivative, prepared by reaction of quinone (V) with o-phenylenediamine, melted at 194°. Derivatives of o-quinones (VI), (XIX), (XX) were prepared in similar fashion from azo compounds (XIII)-(XVIII). Their melting points were identical with those of the phenazine derivatives of o-quinones (VI), (XIX), (XX) described in the preceding paper [1].

SUMMARY

1. It was shown that bromination of derivatives of 5-hydroxynaphthofuran by dioxane dibromide and bromosuccinimide leads to formation of derivatives of 4-bromo-5-hydroxynaphthofuran. The action of dioxane dibromide and bromosuccinimide on substituted 5-hydroxyindoles under similar conditions is more complex, compounds free of bromine as well as resinous polymers being formed.

2. Azo dyes were obtained in good yield by azo coupling of derivatives of 5-hydroxynaphthofuran with diazonium salts.

*Only in this experiment was o-quinone (V) obtained free of impurities. In other experiments it was characterized in the form of the phenazine derivative.

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SYNTHESIS AND RESOLUTION OF STEREOISOMERS OF ASYMMETRIC COMPOUNDS WITH LOCAL ANESTHETIC ACTIVITY

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4035-4038, December, 1960
Original article submitted January 26, 1960

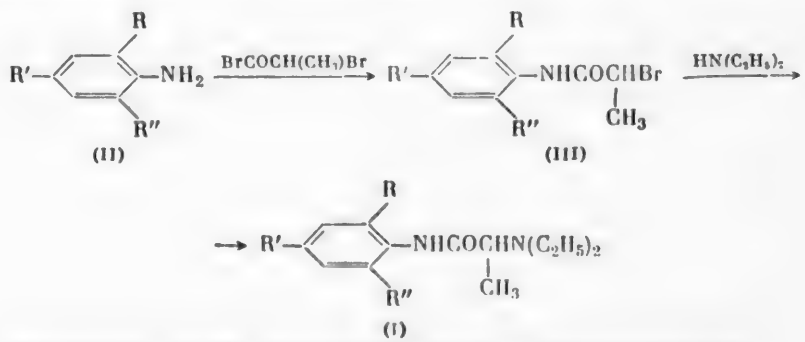
Many cases are known of differences between the biological activity of the levo and dextro isomers of asymmetric compounds. This is due to the proteins of the living organism being levorotatory, so that steric factors will influence their interaction in different ways with the dextro and levo isomers of a biologically active substance.

Many compounds possess local anesthetic activity, but no reliable data are available about the mechanism of their action [1]. It has been stated that the local anesthetic activity of a substance depends only on its physicochemical properties and that it does not enter into a reaction of any sort with proteins of the organism [2]. Other authors assert that the mechanism of local anesthetic action resolves itself into chemical reaction of the substance with the proteins participating in the transmission of nerve impulses [3]. A comparative investigation of the local anesthetic activity of optical isomers of asymmetric compounds might help to some extent in solving this problem.

Only three studies of the local anesthetic activity of optically active stereoisomers are known, and two of these [4, 5] are concerned with isomers of cocaine and eucaine, i.e., substances containing more than one asymmetric carbon atom. The third article [6] alone considers a compound (diothane) containing one asymmetric carbon atom, but the investigation of the local anesthetic activity was inadequate.

Making use of our data for the local anesthetic activity of some arylamides of dialkylaminoacetic acids [7], we synthesized compounds with the general formula (I), which contain a single asymmetric carbon atom.

These compounds were synthesized by the following route:



(II) (III) (I)

a) R = R″ = H, R′ = CH3; b) R = R′ = CH3, R″ = H; c) R = R″ = CH3, R′ = H

Reaction of amine (II) with α-bromopropionyl bromide in acetic acid gave the bromopropionyl derivatives (III), which were then brought into reaction with diethylamine.

Resolution of the optical antipodes of the bases was carried out with the help of D-tartaric acid. The resulting bitartrates were recrystallized 2-3 times from water or alcohol until the angle of rotation was constant. The bases were isolated by treatment of the aqueous solutions of the salts with concentrated ammonia or 20% NaOH solution. Treatment of the filtrate (after separation of one isomer) with alkali enabled isolation of the second isomer slightly contaminated with the first isomer.

Pharmacological tests were performed with hydrochlorides of the racemates as well as of the optically active bases. Salts were prepared by reaction of an ethereal solution of the base with the calculated quantity of alcoholic solution of hydrogen chloride.

The results of the investigation showed that levorotatory isomers are slightly superior in local anesthetic activity to the dextrorotatory.

P. E. Motovilov carried out the comparative study of the local anesthetic activity of the hydrochlorides, and we express our thanks to him.

EXPERIMENTAL

Preparation of amides of α-bromopropionic acid. To a solution of 0.5 mole of amine dissolved in 400 ml of glacial acetic acid and cooled to 10° was added 0.55 mole of α-bromopropionyl bromide, and then 165 g of sodium acetate in 700 ml of water. The precipitate was filtered, washed with water, dried, and recrystallized from aqueous alcohol. In this way we prepared the bromopropionyl derivatives of: a) p-toluidine, m.p. 128-129°, yield 64.5% [8]; b) 2,4-dimethylaniline, m.p. 164-165°, yield 66.2% [9]; c) 2,6-dimethylaniline, m.p. 171-172°, yield 65.5% [10].

Amination of amides of α-bromopropionic acid. A mixture of 0.17 mole of the α-bromopropionyl derivative of the amine, 200 ml of anhydrous benzene, and 50 ml of diethylamine was heated on a glycerol bath at 90-100° (bath temperature) for 5-8 hr. Diethylamine hydrobromide was filtered off and washed with anhydrous benzene. The benzene was distilled off and the residue recrystallized in vacuo. The following substances were obtained (I):

a) α-Diethylaminopropionyl-4-methylanilide, b.p. 142-145° (2 mm), yield 84.5%

Found %: C 72.00; H 9.53; N 12.08. $C_{14}H_{22}ON_2$. Calculated %: C 71.75; H 9.46; N 11.96.

b) α-Diethylaminopropionyl 2,4-dimethylanilide, b.p. 162-163° (2.5 mm), yield 89.6%

Found %: C 72.43; H 9.92; N 11.37. $C_{15}H_{24}ON_2$. Calculated %: C 72.54; H 9.74; N 11.28.

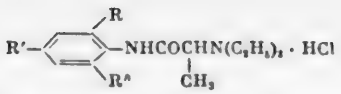
c) α-Diethylaminopropionyl-2,6-dimethylanilide, b.p. 175-176° (5 mm), yield 81% [10].

Resolution of α-diethylaminopropionyl-4-methylanilide. To a solution of 16.2 g of D-tartaric acid in 50 ml of water was added dropwise (with shaking) 25.4 g of the racemic base. A salt came down on standing and was filtered and recrystallized from alcohol until its angle of rotation was constant. M.p. 104-110°, $[\alpha]^{21°}D$ + 2.18° in 15% methanol solution.

Resolution of α-diethylaminopropionyl-2,4-dimethylanilide. To a solution of 24.9 g of D-tartaric acid in 67 ml of water was gradually added, with shaking, 38.74 g of the racemic base. The mass was left overnight. The precipitated salt was filtered, washed with ether, and recrystallized from water to constant angle of rotation; m.p. 90-92°, yield 29.04 g; $[\alpha]^{20.5°}D$ + 8.55° in 15% methanol solution.

The salt was dissolved in water and treated with 20 ml of concentrated ammonia. After extraction with ether, drying of the extract with potassium carbonate, and distillation of the ether, the residue was distilled in vacuo. B.p. 153-156° (3.5 mm), yield of base 13.5 g (70.2%), $[\alpha]^{25°}D$ −34.73° in 15% methanol solution.

Treatment with ammonia of the filtrate after separation of the bitartrate of the levorotatory base yielded the base with b.p. 142-144° (1.5 mm) and $[\alpha]^{22°}D$ + 25.91° in 15% methanol solution.



R	R′	R″	Specific rotation of base	Melting point	Found, %		Empirical formula	Calc., %	
					Cl	N		Cl	N
H	CH_3	H	+15.62°	196–198°	13.05	10.10	$C_{14}H_{22}ON_2 \cdot HCl$	13.09	10.34
CH_3	CH_3	H	−34.73	157–159	12.52	9.74	$C_{15}H_{24}ON_2 \cdot HCl$	12.44	9.83
CH_3	CH_3	H	+25.91	157–158	12.61	9.92	$C_{15}H_{24}ON_2 \cdot HCl$	12.44	9.83
CH_3	H	CH_3	−14.57	237–238	12.33	9.42	$C_{15}H_{24}ON_2 \cdot HCl$	12.44	9.83
CH_3	H	CH_3	+13.59	232–233.5	12.21	9.52	$C_{15}H_{24}ON_2 \cdot HCl$	12.44	9.83

Resolution of α-diethylaminopropionyl-2,6-dimethylanilide. To a solution of 12.56 g of D-tartaric acid in 32 ml of water was gradually added, with shaking, 19.60 g of racemic base dissolved in 25 ml of alcohol. A precipitate came down at once. After heating for 10 min on the water bath, the mass was allowed to stand overnight. The precipitate was then filtered and recrystallized from alcohol until the angle of rotation was constant. $[\alpha]^{16}D$ + 0.98° in 3% aqueous solution; m.p. 89-93°.

The salt was dissolved in water and treated with 20% NaOH solution. The colorless precipitate was filtered, washed with water, and dried in a desiccator; m.p. 61-64°, yield 6.73 g (68.6%), $[\alpha]^{16}D$ −14.57 in 15% methanol solution.

After the bitartrate of the levorotatory base had been separated, the filtrate was evaporated to a viscous, jelly-like mass which did not crystallize after prolonged standing. Treatment with 20% NaOH solution led to separation of the base with m.p. 59-61°, yield 6.0 g (61.2%), $[\alpha]^{18}D$ + 13.59° in 15% methanol solution.

Preparation of hydrochlorides of the salts. To a cooled solution of 5 g of base in 60 ml of absolute ether was added the calculated quantity of ~10% HCl solution in anhydrous alcohol. The precipitate was filtered, washed with absolute ether, recrystallized from absolute acetone, and precipitated with absolute ether. The product was dried in a desiccator. Yield nearly quantitative. The following were prepared:

a) Hydrochloride of racemic α-diethylaminopropionyl-4-methylanilide, m.p. 191-192°.

Found %: N 10.21; Cl 13.09. $C_{14}H_{22}ON_2 \cdot HCl$. Calculated %: N 10.34; Cl 13.09.

b) Hydrochloride of racemic α-diethylaminopropionyl-2,4-dimethylanilide, m.p. 159-161°.

Found %: N 9.86; Cl 12.48. $C_{15}H_{24}ON_2 \cdot HCl$. Calculated %: N 9.83; Cl 12.44.

c) Hydrochloride of racemic α-diethylaminopropionyl-2,6-dimethylanilide, m.p. 231-233° [10].

The hydrochlorides of the optically active isomers were prepared by the same method (see table).

SUMMARY

1. Three arylamides of α-diethylaminopropionic acid were synthesized, two of them for the first time. They were resolved into their optical antipodes with the help of D-tartaric acid.

2. Comparative pharmacological tests showed that all the synthesized compounds possess local anesthetic activity, and that the levorotatory isomers were slightly more active than the dextrorotatory. This difference was greatest with the isomers of α-diethylaminopropionyl-2,4-dimethylanilide which have the highest specific rotation.

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INVESTIGATIONS IN THE FIELD OF SYNTHETIC DYES

XIX. STYRYLS FROM DERIVATIVES OF N-ARYLQUINALDINIUM QUATERNARY SALTS

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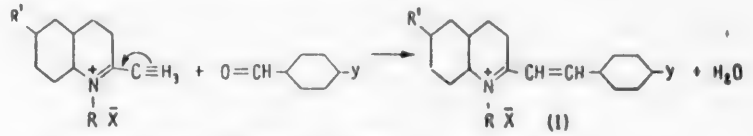
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4038-4041, December, 1960
Original article submitted January 18, 1960

Styryl dyes [1] have been synthesized by condensation of organic carbonyl-containing compounds with cyclammonium bases containing an active methyl group. A series of compounds of this class were later prepared which found application as sensitizers and desensitizers [2-6].

Continuing our work on condensation of N-arylquinaldinium quaternary salts [7-11], we carried out the synthesis of p-aminostyryls and p-dimethylaminostyryls from N-arylquinaldinium quaternary salts. The preparation and investigation of such styryls were of interest because the field has not previously been explored. Due to the presence of an electrophilic radical at the nitrogen atom, the hydrogen atoms of the methyl group in the α-position are here more labile than in alkylhalides of quinaldine, lepidine, benzothiazole and imidazole [12], and therefore the styryls were formed with relative facility.

The condensation involved the following mechanism:



(I)

R = C_6H_5, $C_6H_4CH_3$ (p), $C_{10}H_7$ (α, β); R' = CH_3, H; X = I, ClO_4; Y = NH_2, $N(CH_3)_2$.

We see from the table that dyes with a dialkylamino group in the para-position exhibit an absorption maximum at a wavelength 10-20 mμ larger than in the case of amino derivatives. This is accounted for by the more pronounced nucleophilic properties of the dimethylamino derivatives and by the lower energy level of the molecules of these dyes at the instant of excitation in comparison with amino-substituted styryls. Dyes of the p-aminostyryl series with a phenyl or β-naphthyl radical at the heteronitrogen atom, also their substituted derivatives, have their absorption maximum shifted in the direction of the short-wave region by a uniform amount (6 mμ) after introduction of a methyl group into the 6-position or of a phenylene group into the 5,6-position. When an α-naphthyl radical is attached to the heteronitrogen, the absorption maximum of the dyes is displaced toward the long-wave region in relation to dyes containing phenyl and β-naphthyl radicals. However in this case also, the methyl group in the 6-position induces a hypsochromic shift. In the p-dimethylaminostyryl series an α-naphthyl radical at the heteronitrogen causes a bathochromic shift of the absorption maximum relative to phenyl and β-naphthyl radicals.

Heterocycle	R	Y	X	λ_{max} in ethanol* (mμ)
Quinoline	C_6H_5	NH_2	ClO_4	536
Quinoline	C_6H_5	$N(CH_3)_2$	ClO_4	546 [7]
5,6-Benzoquinoline	C_6H_5	NH_2	I	530
5,6-Benzoquinoline	C_6H_5	$N(CH_3)_2$	I	552 [8]
Quinoline	$C_{10}H_7$-α	NH_2	I	544
Quinoline	$C_{10}H_7$-α	$N(CH_3)_2$	I	560
5,6-Benzoquinoline	$C_{10}H_7$-β	NH_2	ClO_4	530
5,6-Benzoquinoline	$C_{10}H_7$-β	$N(CH_3)_2$	ClO_4	548
5,6-Benzoquinoline	$C_6H_4CH_3$-p	NH_2	I	530
5,6-Benzoquinoline	$C_6H_4CH_3$-p	$N(CH_3)_2$	I	546 [9]
6-Methylquinoline	$C_6H_4CH_3$-p	NH_2	ClO_4	530
6-Methylquinoline	$C_6H_4CH_3$-p	$N(CH_3)_2$	ClO_4	543
6-Methylquinoline	$C_{10}H_7$-α	NH_2	ClO_4	540
6-Methylquinoline	$C_{10}H_7$-α	$N(CH_3)_2$	ClO_4	556

*Spectra were taken with the SF-2M spectrophotometer.

EXPERIMENTAL

(1-Phenylquinolyl-2)-p-aminostyryl perchlorate. A mixture of 1 g of 1-phenylquinaldinium perchlorate, 0.38 g of p-aminobenzaldehyde, and 5 ml of pyridine was refluxed in a small conical flask for 60 min. The mass was then transferred to a beaker of water. Crystals of the dye came down after 20 min and were well washed free of pyridine with water during filtration. Yield of styryl 1.33 g (91%). Recrystallization from aqueous alcohol gave black crystals with a greenish metallic sheen; m.p. 285-287° (decomp.).

Found %: N 6.35. $C_{23}H_{19}O_4N_2Cl$. Calculated %: N 6.60.

(1-Phenyl-5,6-benzoquinolyl-2)-p-aminostyryl iodide. The dye was prepared as in the first case from equimolar quantities of 1-phenyl-5,6-benzoquinaldinium iodide and p-aminobenzaldehyde. Dark crystals with a reddish metallic sheen, m.p. 295° (decomp.). Yield 81% after recrystallization from aqueous alcohol.

Found %: N 5.40, 5.32. $C_{27}H_{21}N_2I$. Calculated %: N 5.59.

(1-α-Naphthylquinolyl-2)-p-aminostyryl iodide. Synthesized by gentle boiling for 50 min of 1 g of 1-α-naphthylquinaldinium iodide and 0.3 g of p-aminobenzaldehyde in 5 ml of pyridine. After an hour the dye was filtered and washed with water and ether. Recrystallization of the styryl from alcohol gave dark crystals with a violet sheen, melting (with decomp.) at 304°. Yield 1.12 g (91%).

Found %: N 5.47, 5.39. $C_{27}H_{21}N_2I$. Calculated %: N 5.59.

(1-α-Naphthylquinolyl-2)-p-dimethylaminostyryl iodide. A mixture of 0.2 g of 1-α-naphthylquinaldinium iodide, 0.07 g of p-dimethylaminobenzaldehyde, and 2 ml of pyridine was gently refluxed in a small flask for 30 min. The content of the flask was then transferred to a beaker of water which on stirring deposited crystals of the dye. These were filtered and washed with water and ether. Yield 0.1 g (37%). Recrystallization gave fine, dark crystals with a violet sheen; m.p. 255° (decomp.).

Found %: N 5.17, 5.21. $C_{29}H_{25}N_2I$. Calculated %: N 5.35.

(1-p-Tolyl-5,6-benzoquinolyl-2)-p-aminostyryl iodide. A mixture of 0.4 g of 1-p-tolyl-5,6-benzoquinaldinium iodide, 0.12 g of p-aminobenzaldehyde, and 2.5 ml of pyridine was boiled on an oil bath (140°) for 50 min. The next day the crystals of styryl were filtered, well washed with water and ether, and recrystallized from alcohol. The dye consisted of a dark-violet, finely crystalline powder, melting (decomp.) at 254°. Yield 0.4 g (77%).

Found %: N 5.28, 5.21. $C_{28}H_{23}N_2I$. Calculated %: N 5.44.

(1-β-Naphthyl-5,6-benzoquinolyl-2)-p-aminostyryl perchlorate. 1-β-Naphthyl-5,6-benzoquinaldinium perchlorate (0.5 g), p-aminobenzaldehyde (0.14 g), and pyridine (3 ml) were heated on a paraffin wax bath for 50 min at 120°. The product was worked up as before to give dark crystals of dye with m.p. 214° (decomp), yield 0.52 g (81%).

Found %: N 5.15, 5.10. $C_{31}H_{27}O_4N_2Cl$. Calculated %: N 5.35.

(1-β-Naphthyl-5,6-benzoquinolyl-2)-p-dimethylaminostyryl perchlorate. A mixture of 0.5 g of 1-β-naphthyl-5,6-benzoquinaldinium perchlorate, 0.18 g of p-dimethylaminobenzaldehyde, and 3 ml of pyridine was refluxed in a small flask for 40 min. The content of the flask was then transferred to a beaker of water and stirred. The dye came down at the bottom of the beaker in the form of a resin which was thoroughly washed free of pyridine with water and ether, and recrystallized from aqueous alcohol. Dark-violet crystals, melting (decomp) at 134-135°. Yield 0.51 g (75%)

Found %: N 4.90, 4.85. $C_{33}H_{27}O_4N_2Cl$. Calculated %: N 5.08.

(1-p-Tolyl-6-methylquinolyl-2)-p-aminostyryl perchlorate. A mixture of 0.5 g of 1-p-tolyl-6-methylquinaldinium perchlorate, 0.18 g of p-aminobenzaldehyde, and 3 ml of pyridine was gently boiled for 50 min on a paraffin wax bath. The dye was filtered, washed with water and ether, and recrystallized from aqueous alcohol. There was obtained 0.58 g (85%) of dark-green crystals with m.p. 240° (decomp.).

Found %: N 5.96, 6.12. $C_{25}H_{23}O_4N_2Cl$. Calculated %: N 6.21.

(1-p-Tolyl-6-methylquinolyl-2)-p-dimethylaminostyryl perchlorate. A mixture of 0.3 g of 1-p-tolyl-6-methylquinaldinium perchlorate, 0.13 g of p-dimethylaminobenzaldehyde, and 3 ml of pyridine was boiled in a small flask for 30 min. The mass was then transferred to a beaker of water and thoroughly stirred. The dye came down as a resin which was washed free of pyridine with water and ether. Recrystallization from alcohol gave 0.2 g (43%) of dark-violet dye with m.p. 258° (decomp.).

Found %: N 5.60, 5.67. $C_{27}H_{27}O_4N_2Cl$. Calculated %: N 5.84.

(1-α-Naphthyl-6-methylquinolyl-2)-p-aminostyryl perchlorate. A mixture of 0.5 g of 1-α-naphthyl-6-methylquinaldinium perchlorate, 0.16 g of p-aminobenzaldehyde, and 4 ml of pyridine was gently boiled for 50 min. The precipitated styryl was filtered and washed with water and ether. Yield 0.6 g (90%). On recrystallization the styryl formed dark-violet crystals with m.p. 259° (decomp.).

Found %: N 5.58, 5.61. $C_{28}H_{23}O_4N_2Cl$. Calculated %: N 5.75.

(1-α-Naphthyl-6-methylquinolyl-2)-p-dimethylaminostyryl perchlorate. A mixture of 0.4 g of 1-α-naphthyl-6-methylquinaldinium perchlorate, 0.15 g of p-dimethylaminobenzaldehyde, and 3 ml of pyridine was refluxed in a conical flask for 30 min. The content of the flask was transferred to a beaker of water and stirred. The fine, dark crystals were filtered and washed with water and ether. After recrystallization from alcohol the styryl melted (with decomp.) at 162-164°.

Found %: N 5.24, 5.31. $C_{30}H_{27}O_4N_2Cl$. Calculated %: N 5.44.

SUMMARY

1. Condensation of N-arylquinaldinium salts, containing an active methyl group in the α-position, with p-aminobenzaldehyde and p-dimethylaminobenzaldehyde gave 11 styryl dyes which have not been described in the literature.

2. Absorption curves of these dyes in the visible spectrum were plotted. The absorption maximum suffers a bathochromic shift of 10-20 mμ when the amino group is replaced by a dialkylamino group.

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REACTIONS OF MAGNESYLAMINES

IX. SYNTHESIS AND CONVERSION OF ARYLIDES OF MANDELIC ACID

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4042-4044, December, 1960
Original article submitted January 29, 1960

Arylides of mandelic acid possess anticonvulsant activity [1]. They are also employed for the synthesis of derivatives of isoquinoline [2] and 3-phenyloxyindole [3] with spasmolytic and analgesic activity. Arylides of mandelic acid can be prepared by reaction of arylamines with acetylmandelyl chloride followed by detachment of the acetyl group [1]; in some cases they are also obtained by direct heating of mandelic acid with aromatic amines [4]. Less important is the reaction of amines with mandelic acid azide [5].

It was earlier shown that mandelic acid anilide can be prepared with good results by reaction of N,N-bis-(bromomagnesium)aniline with ethyl mandelate [6].

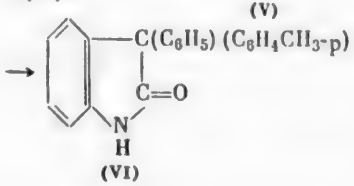
The present investigation was undertaken with the objective of extending the scope of the latter method and of further utilizing arylides of mandelic acid in organic synthesis.

Experiments showed that our method [6] is applicable to preparation of both primary and secondary arylides of mandelic acid. Attainment of maximum yields of mandelic acid arylides requires 1.5 moles of the dimagnesylamine, and in the case of secondary amines it requires 3 moles of monomagnesylamine per mole of ester (Table 1). A certain excess of magnesylamine is needed for reaction with the hydroxy group of the ester.

Starting from mandelic acid arylides (I) we carried out the following reactions:

$$RNHCOCH(OH)C_6H_5 \xrightarrow{O} RNHCOCOC_6H_5$$
(I) (II)

$$C_6H_5NHCOCOC_6H_5 \xrightarrow[(IV)]{p\text{-}CH_3C_6H_4MgBr} C_6H_5NHCOC(OH)(C_6H_5)(C_6H_4CH_3\text{-}p) \xrightarrow{H_2SO_4}$$
(III) (V)



(VI)

Treatment of amides (I) with chromic oxide in acetic acid led to good yields of arylides of benzoylformic acid (II) (phenylglyoxylic acid) (Table 2).

According to the literature the arylides of phenylglyoxylic acid can be obtained by the action of phosphorus pentachloride on benzil monoxime [8], by heating aryl diisocyanates with benzoyl chloride and subsequent hydrolysis of the product [10], and by the action of organomagnesium compounds on hydroxyarylides [11]. Oxidation of mandelic acid arylides is more convenient than the older methods for preparation of arylides of phenylglyoxylic acid.

TABLE 1

Mandelic Acid Arylides $C_6H_5CH(OH)CONHR$

R	Melting point	Yield (%)
$p\text{-}CH_3OC_6H_4$	153—154° [1]	71.3
$p\text{-}CH_3C_6H_4$	172 [7]	94.2
$o\text{-}CH_3C_6H_4$	71—72 [7]	65.3
$p\text{-}ClC_6H_4$	165—166 [1]	83.5
$C_6H_5CHCH_3$ *	114	76.6
$C_6H_5(OH)CON(C_2H_5)C_6H_5$	105—106 **	81.2

*Found %: N 5.41, 5.35. $C_{16}H_{17}O_2N$. Calculated %: N 5.49.

**Literature [1]: m.p. 68-69°.

Due to the presence of a ketonic group in phenylglyoxylic acid arylides, phenylglyoxylic acid anilide (III) reacts with p-tolylmagnesium bromide (IV) to form 4-methylbenzylic acid anilide (V). This reaction is interesting in that it leads to anilides of diarylglycolic acids containing different aryl radicals.

Under the action of concentrated sulfuric acid, anilide (V) is easily converted into 3-phenyl-3-(p-tolyl)-oxindole (VI).

The synthesis of compounds of the type of (V) may present interest for the study of the halochromy of arylides of hydroxycarboxylic acids [12], and also as starting substances for preparation of 3,3-diaryl derivatives of oxindole containing various aryls.

EXPERIMENTAL

Preparation of phenylglyoxylic acid arylides (II). To a stirred and cooled (not above 30°) solution of 0.1 mole of

TABLE 2

Arylides of Phenylglyoxylic Acid $RNHCOCOC_6H_5$

R	Melting point	Appearance (crystallization solvent in parentheses)	Yield (%)
C_6H_5	63—64° [8]	Yellow needles (from aqueous alcohol)	88.2
$p\text{-}CH_3C_6H_4$	112—113 [9]	Yellow platelets (from alcohol)	69.4
$o\text{-}CH_3C_6H_4$	107—108 [10]	Yellow platelets (from alcohol)	78.1
$p\text{-}CH_3OC_6H_4$	123*	Yellow prisms (from aqueous alcohol)	73.6

*Found %: N 5.36, 5.49. $C_{15}H_{15}O_3N$. Calculated %: N 5.45.

**With participation of students A. A. Balakireva, Z. P. Pronina, and V. M. Uglovskaya.

arylide (I) in 20 ml of glacial acetic acid was added a solution of 0.07 mole of chromic oxide in 7 ml of water. The temperature was held at 70° until the yellow color changed to green. The reaction mass was poured into 70 ml of water, and the precipitate was filtered and crystallized from a suitable solvent (Table 2).

4-Methylbenzilic acid anilide (V). To the organomagnesium compound prepared from 5.6 g of p-bromotoluene and 0.73 g of magnesium in 20 ml of ether was added a solution of 3.37 g of phenylglyoxylic acid anilide (III) in 15 ml of ether. The mass was heated for 30 min and decomposed with hydrochloric acid. The ether layer was separated, the ether distilled off with steam, and the residue purified. The compound is soluble in ordinary organic solvents. Needles (from gasoline) with m.p. 111-113°. With concentrated sulfuric acid the anilide gives a dark-cherry coloration which disappears on standing. Yield 3.9 g (83%).

Found %: N 4.32, 4.18. $C_{21}H_{19}O_2N$. Calculated %: N 4.42.

3-Phenyl-3-p-tolyloxindole (VI). To a solution of 0.56 g of anilide (V) in 2 ml of glacial acetic acid was added 3 ml of concentrated sulfuric acid. The resulting dark-red color disappeared after standing for a short period. The reaction was terminated when no further coloration appeared on addition of a fresh portion of sulfuric acid. The reaction mass was poured into water; the precipitate was filtered, washed with water, and crystallized from glacial acetic acid. Platelets with m.p. 193-194°. Yield 0.45 g (84.9%).

Found %: N 4.57, 4.39. $C_{21}H_{17}ON$. Calculated %: N 4.68.

SUMMARY

1. The scope of application of magnesylamines for synthesis of mandelic acid arylides was widened.

2. The oxidation of mandelic acid arylides with formation of phenylglyoxylic acid arylides was studied.

3. It was shown that the reaction between organomagnesium compounds and phenylglyoxylic acid arylides can be used for preparation of arylides of diarylglycolic acids containing different aryls. The glycolic acid arylides can be converted by concentrated sulfuric acid into the corresponding 3,3-diaryloxindoles.

4. The arylides of mandelic and phenylglyoxylic acid described in this paper are of pharmacological interest.

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REACTION OF PHOSPHORUS PENTACHLORIDE WITH UNSATURATED HYDROCARBONS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4044-4048, December, 1960
Original article submitted January 28, 1960

In 1894 E. March and J. Gardner [1] reported that camphene enters into reaction with PCl_5 to form a product which after hydrolysis gives camphenylphosphonic acid. Reactions of PCl_5 with styrene, propylene, isobutene and several other unsaturated hydrocarbons were later [2] described. Somewhat later [3] Bulle showed that the product of reaction of PCl_5 with indene gives, after hydrolysis, indenylphosphonic acid. Reactions of ethylenic and acetylenic hydrocarbons with PCl_5 were studied more thoroughly by E. Bergman and A. Bondi [4] who established that the reaction goes easily with some hydrocarbons with formation of addition products which on hydrolysis give unsaturated phosphonic acids. They assumed the following mechanism:

$$RCH{=}CH_2 + PCl_5 \longrightarrow RCHCl - CH_2PCl_4 \xrightarrow{+3H_2O} RCH{=}CHPO(OH)_2.$$

They did not isolate an intermediate product, but noted that at least a double excess of PCl_5 is necessary for good yields.

Later investigators [5-7] made extensive use of the reaction of PCl_5 with unsaturated hydrocarbons for the preparation of unsaturated phosphonic acids and their dichlorides (formed on reaction of the intermediate products with water or SO_2), and it was noted that the intermediate products are not compounds of the type of $RCHClCH_2PCl_4$, but the complexes of the latter with PCl_5. This accounts for the need for reaction with two moles of PCl_5 which was observed by Bergman and Bondi.

Up to now not a single compound of the type of $RCHClCH_2PCl_4 \cdot PCl_5$ or $RCHClCH_2PCl_4$ has been isolated, nor have their properties been studied (cf. [5]).

It seems strange that hydrolysis of this type of compound or their treatment with SO_2 under the mildest conditions should lead to quantitative detachment of HCl with formation only of unsaturated phosphonic acids or their dichlorides, and not of the corresponding β-chlorophosphonic acids or their dichlorides.

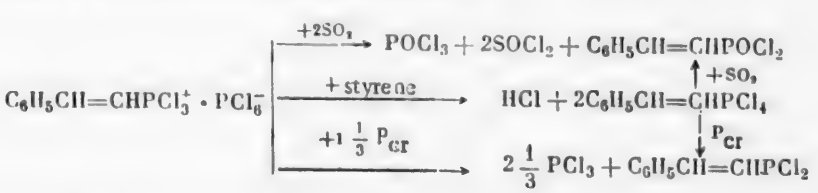
It may be suggested that reaction of PCl_5 with unsaturated hydrocarbons proceeds by another mechanism without formation of derivatives of β-chlorophosphonic acids, namely:

$$RCH{=}CH_2 + PCl_4^+ \longrightarrow [(RCHCH_2PCl_4)^+] \longrightarrow$$

$$\longrightarrow HCl + [RCH{=}CHPCl_3^+] \xrightarrow{+PCl_6^-} RCH{=}CHPCl_3^+ \cdot PCl_6^-$$

The aim of the present work was the preparation in the pure state of the direct products of reaction of PCl_5 with unsaturated hydrocarbons and the clarification of their composition, structure, and chemical properties. The compound selected for the investigation was styrene which reacts with PCl_5 with facility [7]. The reaction takes place at 0° in the course of 6 hr with release of ~1 mole of HCl and with formation of a crystalline, nearly

colorless complex with the structure $C_6H_5CH = CHPCl_3^+ \cdot PCl_6^-$. It was thus proven that, in the case of styrene at least, an intermediate product of the structure $ArCHClCH_2PCl_4 \cdot PCl_5$ [7] is either not formed or is so unstable that it breaks down even at 0°. The reaction goes at a much higher rate at 70°. The yield of complex $C_6H_5CH = CHPCl_3^+ \cdot PCl_6^-$ is about 80%. Styrylphosphonous dichloride [7] is formed in high yield when the complex is reacted with SO_2. With styrene the complex forms styrylphosphorus tetrachloride. On reduction with red phosphorus (cf. [8]) the complex is converted into styryldichlorophosphine.



All these chemical reactions in association with the analytical data provide ample proof of the structure of the complex. When heated, the complex breaks down with formation of HCl, PCl_3, and halogenated hydrocarbons which were not closely examined. The temperature of breakdown depends on the rate of heating of the complex. With slow heating the release of HCl starts at 110° and finishes at 130°.

Styrylphosphorus tetrachloride is a yellow substance crystallizing in large needles, m.p. 65-78° (thermometer bulb in the liquid), very easily decomposed by atmospheric moisture. It could not therefore be isolated in the absolutely pure state. However, the phosphorus content and the results of titration of the products of hydrolysis correspond with sufficient closeness to the composition $C_6H_5CH = CHPCl_4$. Its structure is confirmed by conversion to styrylphosphonous dichloride by reaction with SO_2 and by reduction with red phosphorus to styryldichlorophosphine.

Analogous complexes of the type of $ArPCl_3^+ \cdot PCl_6^-$ were obtained by the action of PCl_5 on arylphosphonous dichlorides.

$$ArPOCl_2 + 2PCl_5 \longrightarrow POCl_3 + ArPCl_3^+ \cdot PCl_6^-$$

The reaction goes at 75-80° in benzene solution with yields of about 70%. The complexes $ArPCl_3^+ \cdot PCl_6^-$ (Ar = C_6H_5 and p-$CH_3C_6H_4$) are slightly yellowish compounds that are easily hydrolyzed by atmospheric moisture. On reduction with red phosphorus they give the corresponding aryldichlorophosphines.

$$3ArPCl_3^+ \cdot PCl_6^- + 4P_{cr} \longrightarrow 3ArPCl_2 + 7PCl_3$$

Arylphosphorus tetrachlorides (Ar = C_6H_5 and p-$CH_3C_6H_4$) are also reduced by red phosphorus to aryldichlorophosphines.

$$3ArPCl_4 + 2P_{cr} \longrightarrow 3ArPCl_2 + 2PCl_3$$

EXPERIMENTAL

Preparation of the complex $C_6H_5CH = CHPCl_3^+ \cdot PCl_6^-$. To a well-stirred solution of 0.2 mole of PCl_5 in 100 ml of benzene at 70-75° (thermometer bulb in liquid) was added a solution of 0.1 mole of styrene in 20 ml of benzene in the course of 10 min. Nearly colorless crystals came down and HCl was released. Stirring of the reaction mixture was continued at 70-75° for 2 hr. During this period 0.094 mole of HCl came off and was collected and determined by the usual method. Performance of the reaction at 0° for 6 hr resulted in release of 0.088 mole of HCl. The complex was suction-filtered from the hot solution (60-70°) in a stream of dry air and washed with benzene; yield 62%.

The complex is sparingly soluble in boiling nonpolar solvents and nearly insoluble in cold; it is rapidly hydrolyzed by atmospheric moisture, and reacts violently with water, alcohols, ammonia, and amines. At 110-130° it breaks down with loss of HCl and PCl_3.

Found %: P 13.15, 13.21. Equiv. after hydrolysis 12.59, 13.40. $C_8H_7P_2Cl_9$ Calculated %: P 12.80. Equiv. after hydrolysis 13.00.

Preparation of styrylphosphorus tetrachloride. To a solution of 0.1 mole of PCl_5 in 100 ml of benzene, stirred at 65-70°, was added a solution of 0.1 mole of styrene in 20 ml of benzene in the course of 10 min. Colorless crystals came down and HCl was liberated. The reaction mixture was stirred for 3 hr at the same temperature. The precipitate gradually dissolved to a green, transparent solution, and a total of 0.097 mole of HCl was evolved. The benzene was taken off in vacuo at 40-50° to leave a yellow liquid which partly crystallized on standing. Yield of crude product 90%. After suction-filtration, the crystalline product melted at 65-78°.

Styrylphosphorus tetrachloride differs from its complex with PCl_5 in being easily soluble in nonpolar solvents.

Found %: P 11.71. Equiv. after hydrolysis 5.74, 5.50. $C_8H_7PCl_4$. Calculated %: P 11.29. Equiv. after hydrolysis 6.00.

Preparation of styrylphosphonous dichloride. a) From the complex $C_6H_5CH = CHPCl^+ \cdot PCl_6^-$. Sulfur dioxide was passed through a mixture of 0.05 mole of the complex and 80 ml of benzene at 3-5° until the crystals disappeared. Benzene and low-boiling products were distilled off in vacuo to leave the slightly yellowish crystalline styrylphosphonous dichloride [7], m.p. 68-70°. Yield theoretical.

b) From styrylphosphorus tetrachloride. The tetrachloride (0.1 mole) was treated with SO_2. The reaction was exothermic. A yellow liquid was formed. The $SOCl_2$ was removed in vacuo and styrylphosphonic dichloride [7] was obtained with m.p. 69-70°. Yield theoretical. B.p. 127-130° (4 mm). Yield of distilled product 84%.

Preparation of styryldichlorophosphine. a) From $C_6H_5CH = CHPCl_4$. A mixture of 0.1 mole of styrylphosphorus tetrachloride and 0.07 g-atom of red phosphorus was heated to 140-160° on an oil bath. The PCl_3 (60%) was distilled off. The excess of red phosphorus was suction-filtered, and the filtrate distilled in vacuo. Yield of styryldichlorophosphine 50%, b.p. 133-135° (7 mm), $n^{19}D$ 1.6355 [8].

Found %: Cl 34.7, 34.84. $C_8H_7PCl_2$. Calculated %: Cl 34.63.

b) From $C_6H_5CH = CHPCl_3^+ \cdot PCl_6^-$. Reaction was effected, by the above procedure, between 0.08 mole of complex and 0.11 g-atom of red phosphorus. Yield of PCl_3 82%; yield of styryldichlorophosphine 52%, b.p. 133-135° (7 mm), $n^{19}D$ 1.6345 [8].

Preparation of $C_6H_5PCl_3^+ \cdot PCl_6^-$ from phenylphosphonous dichloride. To a boiling solution of 0.2 mole PCl_5 in 100 ml of benzene was added a solution of 0.1 mole of phenylphosphonous dichloride in the course of 30 min with stirring. Fine, colorless crystals came down. After the whole of the dichloride had been added, the reaction mixture was stirred for 5 hr at 80°. The precipitate was suction-filtered in a current of dry air. Yield 65%. The complex $C_6H_5PCl_3^+ \cdot PCl_6^-$ is a slightly yellowish, finely crystalline substance rapidly hydrolyzing in the air and having an odor of phosphorus pentachloride. It decomposes on heating (200-220°) without melting.

Found %: P 13.56, 13.52. Equiv. after hydrolysis 12.65, 12.85. $C_6H_5P_2Cl_9$. Calculated %: P 13.52. Equiv. after hydrolysis 13.00.

Preparation of $p\text{-}CH_3C_6H_5PCl_3^+ \cdot PCl_6^-$. The procedure was the same as for the preceding complex. The substance comes out in the form of a greenish oil which crystallizes after a few hours. Yield 75%, m.p. 158-160°.

Found %: P 12.89, 12.60. Equiv. after hydrolysis 12.97, 12.90. $C_7H_7P_2Cl_9$. Calculated %: P 13.12. Equiv. after hydrolysis 13.00.

Preparation of phenyldichlorophosphine. a) From $C_6H_5PCl_4$. A mixture of 0.03 mole of $C_6H_5PCl_4$ and 0.02 g-atom of red phosphorus was heated on an oil bath at 140-155° for 30-40 min, the PCl_3 (80%) being distilled off at the same time. The excess of red phosphorus was suction-filtered and the filtrate distilled in vacuo. Yield of phenyldichlorophosphine 70%, b.p. 80-83° (8 mm), $n^{18}D$ 1.5940 [9].

Found %: P 17.17, 17.86. $C_6H_5PCl_2$. Calculated %: P 17.31.

b) From $C_6H_5PCl_3^+ \cdot PCl_6^-$. A mixture of 0.02 mole of $C_6H_5PCl_3^+ \cdot PCl_6^-$ and 0.03 g-atom of red phosphorus was heated on an oil bath at 100° for 30 min. Yield of PCl_3 82%; yield of $C_6H_5PCl_2$ 78%, b.p. 80-83° (8 mm), $n^{19}D$ 1.5984 [9].

Preparation of p-tolyldichlorophosphine. a) From $p\text{-}CH_3C_6H_4PCl_4$. Procedure as in preceding experiments. Bath temperature 160-170°. Yield of PCl_3 71%; yield of p-tolyldichlorophosphine 84%, b.p. 117-118° (18 mm), $n^{19}D$ 1.5860 [9].

b) From $p\text{-}CH_3C_6H_4PCl_3^+ \cdot PCl_6^-$. The same procedure was employed at a bath temperature of 120-130°. Yield of PCl_3 80%; yield of p-tolyldichlorophosphine 42%, b.p. 108-110° (12 mm), $n^{20}D$ 1.5851 [9].

Found %: P 16.24, 15.68. $C_7H_7PCl_2$. Calculated %: P 16.02.

SUMMARY

1. The complex formed by the action of PCl_5 on styrene has the structure $C_6H_5CH = CHPCl_3^+ \cdot PCl_6^-$ and not $C_6H_5CHClCH_2PCl_4 \cdot PCl_5$ as had been assumed previously. The intermediate unstable reaction product is probably the complex $(C_6H_5CHClCH_2PCl_4)^+ \cdot PCl_6^-$.

2. At 70° the complex $C_6H_5CH = CHPCl_3^+ \cdot PCl_6$ reacts with styrene with formation of styrylphosphorus tetrachloride which with SO_2 gives styrylphosphonous dichloride.

3. Reduction with red phosphorus of complexes of the type of $ArPCl_3^+ \cdot PCl_6^-$ and of compounds of the type of $ArPCl_4$ gives $ArPCl_2$.

4. Treatment of arylphosphonous dichlorides with PCl_5 gives the complexes $ArPCl_3^+ \cdot PCl_6^-$.

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HYDROLYSIS AND ACIDOLYSIS OF MONOMERIC AND DIMERIC TRICHLOROPHOSPHAZOARYLS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4048-4053, December, 1960
Original article submitted January 28, 1960

In the preceding paper it was shown that reaction of PCl_5 with weakly basic aromatic amines gave trichlorophosphazoaryls, ArN = PCl_3, with properties similar to those of trichlorophosphazoacyls. On the other hand reaction of PCl_5 with more strongly basic aromatic amines was found to give dimeric trichlorophosphazoaryls, $(ArN = PCl_3)_2$, with chemical and physical properties diverging considerably from those of trichlorophosphazoacyls.

Monomeric trichlorophosphazoaryls, like trichlorophosphazoacyls, are hydrolyzed with amazing facility by water and atmospheric moisture, and are also acidolyzed by formic and acetic acids to give arylamidophosphoric dichlorides (I)-(Iv) (Table 1). For preparative purposes the acidolysis is most conveniently performed with formic acid in benzene solution.

$$ArN{=}PCl_3 + HCOOH \longrightarrow ArNHPOCl_2 + HCl + CO. \quad (A)$$

In contrast to the reaction with monomeric trichlorophosphazoaryls, hydrolysis or acidolysis of the dimeric compounds does not lead to arylamidophosphoric dichlorides (see below). Treatment with formic acid of solutions or suspensions of dimeric trichlorophosphazoaryls in benzene leads to a violent reaction which is strongly exothermic and is accompanied by release of gases. The product is a viscous, ropy or vitreous mass from which pure substances could not be isolated.

As was shown in the preceding communication [1], some of the dimeric trichlorophosphazoaryls are completely degraded to monomers by boiling of their benzene solutions. Cooling and prolonged standing of the resulting solutions does not lead to dimerization. Treatment of the solutions of monomers with formic acid leads to reaction by Eq. (A) with formation of the dichlorides (V)-(XII) (Table 1).

Arylamidophosphoric dichlorides are colorless, crystalline substances. The nitro compounds (III), (IV), (X)-(XII) are yellow. Compounds (V)-(VI) are easily soluble in benzene, ether, and CCl_4; (I)-(IV) are sparingly soluble in the same solvents in the cold and more soluble when heated. Compound (XII) is sparingly soluble in organic solvents even with heating. Water and moist air rapidly hydrolyze arylamidophosphoric dichlorides. Compounds (X) and (XI) are thereby hydrolyzed with particular facility; this behavior is an obstacle to their isolation in the pure state. The dichlorides slowly decompose when heated for a prolonged period in a solvent or on a water bath without a solvent.

Dichlorides (I), (II), (VII), (IX), (XI), and (XII) were previously obtained by Michaelis [2], but his melting points of the first five members differ considerably from the true one (Table 1). Only for (XII) did Michaelis give the correct melting point. The identity between the dichlorides prepared by Michaelis and the substances formed by partial hydrolysis of trichlorophosphazoaryls was proven by synthesis of 2,4-dichlorophenylamidophosphoric dichloride from 2,4-dichloroaniline and $POCl_3$. The resulting dichloride was identical with substance (VII) and did not give a depressed melting point in admixture with the latter.

TABLE 1

Arylamidophosphoric Dichlorides $ArNHPOCl_2$

Substance No.	Ar	Yield (%)	Melting point	Empirical formula	Found			Calculated •	
					% Cl ••	equiv.	M •••	% Cl ••	M
I	$2,4,6\text{-}Cl_3C_6H_2$	79	156–158° ••••	$C_6H_3ONPCl_5$	22.44, 22.57	3.97, 4.02	323, 336	22.65	313.5
II	$2,4,6\text{-}Br_3C_6H_2$	86	186–188 ••••	$C_6H_3ONCl_2PBr_3$	15.60, 15.73	3.92, 3.92	421, 463	15.66	447
III	$2,4\text{-}(NO_2)_2C_6H_3$	77	121–122	$C_6H_4O_5N_3PCl_2$	23.86, 23.57	—	295, 283	23.88	300
IV	$2,6\text{-}Cl_2\text{-}4\text{-}NO_2C_6H_2$	89	171–173	$C_6H_3O_3N_2PCl_4$	21.63, 21.72	—	329, 302	21.91	324
V	$o\text{-}ClC_6H_4$	100	77–79	$C_6H_5ONPCl_3$	29.63, 29.65	3.97, 4.00	216, 254	29.04	244.5
VI	$o\text{-}BrC_6H_4$	100	82–83	$C_6H_5ONCl_2PBr$	25.04, 25.19	4.23, 4.26	280, 275	24.57	289
VII	$2,4\text{-}Cl_2C_6H_3$	100	98–100 ••••	$C_6H_4ONPCl_4$	25.26, 25.17	4.00, 4.02	294, 287	25.45	279
VIII	$3,5\text{-}Cl_2C_6H_3$	100	117–118	$C_6H_4ONPCl_4$	25.07, 25.12	4.01, 3.96	288, 262	25.45	279
IX	$2,4\text{-}Br_2C_6H_3$	100	96–98 ••••	$C_6H_4ONCl_2PBr_2$	19.32, 19.05	3.89, 3.94	351, 345	19.29	368
X	$o\text{-}NO_2C_6H_4$	93	40–42	$C_6H_5O_3N_2PCl_2$	27.00, 27.02	—	240, 259	27.84	255
XI	$m\text{-}NO_2C_6H_4$	84	88–90 ••••	$C_6H_5O_3N_2PCl_2$	27.04, 27.26	—	279, 267	27.84	255
XII	$p\text{-}NO_2C_6H_4$	82	155–156 •••••	$C_6H_5O_3N_2PCl_2$	—	—	—	—	—

•Calculated equiv. 4.00.

••Hydrolyzable chlorine.

•••Cryoscopically in benzene.

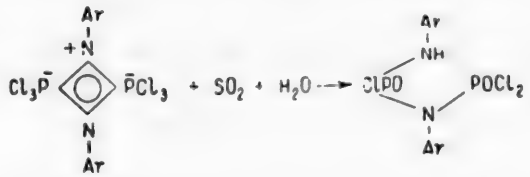
••••According to Michaelis [2] substance (I) melts at 128°, (II) at 148°, (VII) at 126°, and (IX) at 148°. These are inaccurate.

•••••According to Michaelis [2] b.p. 156°.

Arylamidophosphoric dichlorides are converted by PCl_5 in good yields into the original monomeric or dimeric trichlorophosphazoaryls (cf. [1]):

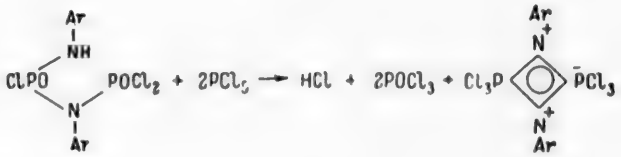
$$ArNHPOCl_2 + PCl_5 \rightarrow POCl_3 + HCl + ArN{=}PCl_3.$$
$$2ArNHPOCl_2 + 2PCl_5 \rightarrow 2POCl_3 + 2HCl + (ArN{=}PCl_3)_2$$

Of great interest for the elucidation of the structure of dimeric trichlorophosphazoaryls is their partial hydrolysis without depolymerization. Dimeric trichlorophosphazoaryls were treated under the most diverse conditions with water, concentrated hydrochloric acid, moist air, partially hydrolyzed $POCl_3$, formic acid, and acetic acid. In no instance were products of partial hydrolysis of dimeric trichlorophosphazoaryls isolated in the pure state. Products of partial hydrolysis which had not suffered scission of the molecule were isolated only after hydrolysis of four of the more difficultly depolymerizable trichlorophosphazoaryls under special conditions—treatment with wet SO_2 of a suspension of the substance in $POCl_3$. Judging by elemental composition, molecular weight, and chemical properties, these substances are N,N'-diaryl-N-dichlorophosphonyldiamidophosphoric dichlorides (Table 2).



All of the remaining dimers of trichlorophosphazoaryls are converted by moist sulfur dioxide into viscous resins with a dirty-yellow color from which individual substances could not be isolated.

N,N'-Diaryl-N-dichlorophosphonyldiamidophosphoric dichlorides are colorless, crystalline compounds, insoluble in benzene, ether, CCl_4, and ligroine, easily soluble in dioxane and $POCl_3$. They are fairly stable in the crystalline state, but decompose very quickly when heated in organic solvents or $POCl_3$. The structure of these dichlorides was confirmed by their conversion, when treated with 2 moles of $POCl_3$, into the original dimeric trichlorophosphazoaryls:



EXPERIMENTAL

Arylamidophosphoric dichlorides (I)-(IV) from monomeric trichlorophosphazoaryls. To a solution of 0.1 mole of trichlorophosphazoaryl in 100 ml of anhydrous benzene was added 0.1 mole of anhydrous formic acid dropwise with shaking. The precipitated arylamidophosphoric dichloride was suction-filtered, washed with benzene, and dried in vacuo. Compounds (II)-(IV) were recrystallized from benzene, and (I) was recrystallized from CCl_4.

Arylamidophosphoric dichlorides (V)-(XII) from dimeric trichlorophosphazoaryls. A solution of trichlorophosphazoaryl was prepared by refluxing 0.01 mole in anhydrous benzene. The amount of benzene was 50 ml for compounds (V)-(VII), (X), (XII), 80 ml for compound (VIII), and 200 ml for compound (XI). Some of the dimeric trichlorophosphazoaryls dissolved very slowly in boiling benzene (15-20 min). The benzene solution was cooled to room temperature and 0.01 mole of anhydrous formic acid was added dropwise with shaking. After completion of the reaction, the solution was at once evaporated in vacuo at room temperature. Prolonged standing of the solutions is not recommended. The arylamidophosphoric dichlorides gradually come down in the form of colorless crystals. Compounds (X) and (XI) at first separate as light-yellow oils, but these crystallize later. Compound (XII) is sparingly soluble in benzene and gradually comes down in the course of formation. Arylamidophosphoric dichlorides were purified by crystallization from a mixture of benzene and ligroine. The easily hydrolyzed compounds (X) and (XI) were not subjected to crystallization.

TABLE 2

N,N'-Diaryl-N-dichlorophosphonyldiamidophosphoric Dichlorides ArNHPO(Cl)NAr($POCl_2$)

Substance No.	Ar	Yield (%)	Melting point	Empirical formula	Found				Calc.	
					% Cl	equiv. after hydrolysis	M **		% Cl	M
							in benzene	in dioxane		
XIII	C_6H_5	70	139—141°	$C_{12}H_{11}O_2N_2Cl_3P_2$	27.43, 27.22	6.96, 6.99	—	372, 350	27.77	383.5
XIV	p-ClC_6H_4	60	149—151	$C_{14}H_{15}O_2N_2Cl_3P_2$	26.40, 26.24	7.05, 7.04	420, 401	385, 378	25.93	411.5
XV	p-BrC_6H_4	58	148—150	$C_{12}H_{10}O_2N_2Cl_3Br_2P_2$	19.83, 20.10	7.01, 7.03	535, 520	551, 559	19.66	541.5
XVI	3,5-$(CH_3)_2C_6H_3$	94	160—162	$C_{16}H_{17}O_2N_2Cl_3P_2$	24.08, 24.04	6.85, 6.99	443, 443	—	24.23	439.5

* Calculated equivalent after hydrolysis 7.00.

** Cryoscopically.

N,N'-Diaryl-N-dichlorophosphonyldiamidophosphoric dichlorides (XIII)-(XVI). A fairly rapid stream of SO_2 was passed into a suspension of 0.1 mole of dimeric trichlorophosphazoaryl in 100 ml of $POCl_3$. The SO_2 was previously passed in turn through a sulfuric acid wash bottle, a phosphorus pentoxide column, and a small flask containing 0.1 mole of water, care being taken that the gas-leading tube did not touch the surface of the water. The crystalline dimeric trichlorophosphazoaryl gradually dissolved. The reaction mixture attained a temperature of 40-50° due to the heat of reaction. During preparation of compound (XVI) the flask was externally cooled with ice water. After about an hour the rate of evaporation of the water was accelerated by gradual heating of the water-containing flask to 70-80° on a water bath. The dimeric trichlorophosphazoaryls dissolved completely within 2-3 hr after the start of the reaction, and the liberation of heat by the reaction mixture ceased. Passage of the SO_2 was continued for a further 1-2 hr after all of the dimer had dissolved. The $POCl_3$ was distilled from the transparent, slightly yellowish solution in vacuo at a temperature not exceeding 30-40°. Unreacted dimer was first filtered off when compound (XV) was being prepared. The residue after distillation of the $POCl_3$ was a crystalline substance permeated by oil. It was treated with cold benzene. The crystals were suction-filtered, thoroughly washed several times with benzene and ether, and dried in vacuo.

Reaction of arylamidophosphoric dichlorides with PCl_5. The dichloride (0.02 mole) was dissolved or suspended in CCl_4 [compounds (I), (II), (IV), (XII) in 15 ml, (V)-(XI) in 5 ml], 0.02 mole of PCl_5 was added, and the mixture refluxed until HCl ceased to be evolved (30-40 min). Dichloride (XII) reacts very slowly with PCl_5 (12 hr), due to its poor solubility in CCl_4. In the case of compounds (I), (II), and (IV) the CCl_4 is taken off in vacuo to leave the trichlorophosphazoaryls in the form of oils which soon crystallize, with the exception of the liquid trichlorophosphazo-2,4,6-trichlorobenzene. In the case of compounds (V)-(XI) a transparent solution is obtained from which the dimeric trichlorophosphazoaryl gradually crystallizes. Yields 70-90%. The products were identified by mixed melting point tests with authentic specimens [1]. Only dichloride (III) could not be converted to trichlorophosphazo-2,4-dinitrobenzene by this method. As established earlier [1], trichlorophosphazo-2,4-dinitrobenzene must be prepared at a temperature not exceeding 60° (bath temperature). Dichloride (III) does not react with PCl_5 at 60°. The reaction goes on boiling in CCl_4, but then pure substances cannot be isolated.

Reaction of N,N'-diaryl-N-dichlorophosphonyldiamidophosphoric chlorides with PCl_5. To a suspension of 0.05 mole of chlorides (XIII)-(XVI) in 10 ml of CCl_4 was added 0.1 mole of PCl_5, and the mixture refluxed until HCl ceased to be evolved. The resulting precipitate of dimeric trichlorophosphazoaryl was suction-filtered, washed with CCl_4, and dried in vacuo. Yield of dimer of trichlorophosphazophenyl 84%, of p-trichlorophosphazotoluene 85%, of trichlorophosphazo-p-bromobenzene 26%, and of trichlorophosphazo-3,5-dimethylbenzene 40%. The dimeric trichlorophosphazoaryls were identical with those obtained earlier [1].

SUMMARY

1. Monomeric trichlorophosphazoaryls are easily hydrolyzed to the chlorides of the corresponding arylamidophosphoric acids.

2. Hydrolysis of dimeric trichlorophosphazoaryls does not give the chlorides of arylamidophosphoric acids.

3. Dimeric trichlorophosphazoaryls are completely depolymerized when boiled in benzene solution; treatment of the benzene solutions of the monomers with formic acid leads to the chlorides of arylamidophosphoric acids.

4. Reaction of some dimeric trichlorophosphazoaryls with moist sulfur dioxide gives the chlorides of N,N'-diaryl-N-dichlorophosphonyldiamidophosphoric acids, which react with PCl_5 to form the original dimeric trichlorophosphazoaryls.

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DIPHOSPHONATES

IV. SYNTHESIS OF TETRAALKYL ESTERS OF SOME DIPHOSPHONIC ACIDS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4053-4055, December, 1960
Original article submitted February 2, 1960

Esters of diphosphonic acids have been described mainly in the patent literature [1-4]. They were prepared in connection with the search for high-boiling lubricating oils, oil additives, hydraulic fluids, and inhibitors of oxidation processes. The mechanism of formation of tetraalkyl esters of diphosphonic acids in the Michaelis–Becker reaction has already been investigated [5].

Our present work was concerned with the synthesis of tetraalkyl esters of diphosphonic acids of higher alcohols by the reaction

$$2(RO)_2PONa + Cl(CH_2)_2O(CH_2)_2Cl \longrightarrow (RO)_2\overset{\overset{O}{\|}}{P}(CH_2)_2O(CH_2)_2\overset{\overset{O}{\|}}{P}(OR)_2 + 2NaCl.$$

A solution of sodium dialkyl phosphite in toluene was added to dichlorodiethyl ether heated to 90°. Secondary reaction products (ester salts) were separated by washing the reaction mixture with alkali solution and water; esters of alkylphosphonic acids were separated by heating the product in high vacuum.

The diphosphonates are high-boiling, viscous liquids, crystallizing at 14-22°, poorly soluble in water and readily soluble in ether, acetone, benzene, and other organic solvents. Only the first and second substances (see table) could be distilled [b.p. 240-245° (0.2 mm), 250-255° (0.2 mm)]. The remaining diphosphonates decomposed when distilled and were therefore analyzed without distillation.

Thermal breakdown of diphosphonates by heating for 5 min at 290° was accompanied by formation of the corresponding unsaturated hydrocarbons and by increased acidity of the residue. The degree of decomposition of the diphosphonates was determined from the quantity of 0.1 N alkali solution used for titration of a weighed sample before and after heating.

The experimental and calculated values of molar refraction are in satisfactory agreement with the values for bis(dialkylphosphono)diethyl esters only for a value of 5.01 for the atomic refraction of phosphorus [6].

Dialkyl phosphites of higher alcohols, used as starting substances, were prepared by B. A. Arbuzov's method [7]. The yield of dioctyl phosphite could be raised from 45 to 81% and that of dinonyl phosphite to 83% by use of a solvent and removal of the hydrogen chloride from the sphere of reaction by blowing with dry air.

EXPERIMENTAL

Diethyl bis(diheptylphosphonate) (typical experiment). In the course of 3 hr 0.3 mole of sodium diethyl phosphite (prepared from 0.3 g-atom of sodium and 0.3 mole of diheptyl phosphite in 200 ml of toluene) was stirred into 0.5 mole of dichlorodiethyl ether heated on a water bath to 90-95°. The mixture was refluxed and

Formula	Melting point	Viscosity at 20°	d_4^{20}	n_D^{20}	MR_D		Acidity (as mg KOH)		% P		Yield (%)
					calc.	found	before heating	after heating	calc.	found	
$[(iso\text{-}C_5H_{11}O)_2PCH_2CH_2]_2O$ (=O)	14.0°	36.34	1.0000	1.4503	137.9	138.3	0.33	83.5	12.08	12.1, 12.2	52
$[(n\text{-}C_9H_{19}O)_2PCH_2CH_2]_2O$ (=O)	15.2	51.06	0.9828	1.4520	156.4	157.2	0.62	19.8	10.90	11.2, 11.3	42
$[(n\text{-}C_7H_{15}O)_2PCH_2CH_2]_2O$ (=O)	16.0	63.83	0.9644	1.4530	174.9	175.3	0.13	20.6	9.88	9.9, 10.1	48
$[n\text{-}(C_8H_{17}O)_2PCH_2CH_2]_2O$ (=O)	17.5	76.81	0.9554	1.4550	193.6	193.6	0.06	2.58	9.08	9.1, 9.1	42
$[(n\text{-}C_9H_{19}O)_2PCH_2CH_2]_2O$ (=O)	22.5	45.73 (at 30°)	0.9475	1.4565	211.8	212.2	0.10	5.45	8.38	8.5, 8.6	50
$[(iso\text{-}C_5H_{11}O)_2PCH_2CH_2]_2$ (=O)	—	59.75	0.9986	1.4500	134.7	134.2	0.84	1.33	12.45	12.5, 12.6	34

stirred for 5-9 hr. After cooling, the precipitate was dissolved by addition of water. The organic layer was washed with 10% alkali solution until alkaline to phenolphthalein, and twice washed with water (each time with 50 ml). After drying over calcined sodium sulfate, the solvent was distilled in vacuo, and volatile impurities removed by heating for 30 min at 220° (0.2 mm). The residue of 45.4 g (48.5%) of product melted at 16°.

Test of the thermal stability of diphosphonates. A weighed quantity (0.3 g) of diphosphonate was shaken in a conical flask with 50 ml of water and titrated with 0.1 N alkali solution in presence of phenolphthalein. A second weighed sample of the same substance was placed in a test tube with a side tube connected to a trap at −70°, heated for 5 min at 290°, and titrated with 0.1 N alkali solution in presence of phenolphthalein. The acidity was expressed as milligrams of dry potassium hydroxide consumed in titration (see table).

Dinonyl phosphite. To a stirred solution of 432.7 g of nonyl alcohol in 200 ml of dry carbon tetrachloride, through which dry air was blown, was added 137 g of phosphorus trichloride in the course of 20 min at 70°. The reaction mixture was stirred at the same temperature, with air blowing, for another hour. The content of the flask was then transferred to a Claisen flask and kept at room temperature in the vacuum of a water jet pump, with continued blowing with air, until the gage registered a constant pressure (15-20 mm). Fractionation in vacuo yielded 278 g (83.2%) of substance.

B.p. 200-202° (2 mm), d^{20}_4 0.8982, $n^{20}D$ 1.4420. MR_D 98.54; calc. 98.28. Literature data: b.p. 174.5-175.5° (0.04 mm), d^{20}_4 0.9212, $n^{20}D$ 1.4458 [8].

Found %: P 9.13, 9.15. $C_{18}H_{39}O_3P$. Calculated %: P 9.27.

SUMMARY

1. Five new members of the class of diethyl esters of bis(dialkylphosphonic) acid and the tetraisoamyl ester of tetramethylenediphosphonic acid were described.

2. The method of preparation of dialkyl phosphites of higher alcohols was improved.

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RAMAN SPECTRA OF SOME ESTERS OF DITHIO- AND THIOPHOSPHORIC ACIDS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4056-4057, December, 1960
Original article submitted January 22, 1960

The spectral characteristics of the P = S group of esters of thiophosphonic acid are of interest for establishment of the structure of the molecules and for analytical purposes.

Gore [1] analyzed over 30 infrared spectra of various thiophosphoric and phosphoric compounds and found that thiophosphoric derivatives have a strong band in the 450-600 cm^{-1} region; Melver et al. [2], examined the infrared spectra of 50 organic compounds of phosphorus, but found the P = S bond to be associated with vibrations in the 770-835 cm^{-1} region. Bellamy [3] summarizes his own investigations and other literature data in his monograph [4] in which he correlates the P = S group with absorption in the 600-750 cm^{-1} region. Other authors arrived at similar conclusions [5]. Several papers have been published on the Raman spectra (RS) of thiophosphoric compounds [6] and the 600-650 cm^{-1} frequency has been associated with the P = S bond. On the basis of their own abundant data (IR and RS) E. M. Popov et al. [7] concluded that the frequencies of the P = S group are in the 580-750 cm^{-1} region, but are exposed to the influences of attached groupings, so that they remain constant only when the groupings in the immediate vicinity are unchanged.

We investigated the RS of some mainly acidic esters of dithio- and thiophosphoric acids with the objective of establishing the characteristic frequencies of the P = S group.

The spectra were taken with an ISP-51 spectrograph; F of camera = 270 mm; excitation by the 4538 A line of Hg; width of slit 5 cm^{-1}; exposure period 2 hr.

Esters of dithio- and thiophosphoric acids were prepared by the method of Kabachnik and Mastryukova [8]. Esters of dithiophosphoric acid were purified by Lesuer's method [9] and spectrographed in the freshly distilled condition. Esters of thiophosphoric acid were distilled three times and used on the same day.

Raman Spectra

I. $(CH_3O)_2P(S)SH$: 252 (2), 294 (1), 344 (1), 371 (1), 295 (1), 433 (1), 496 (5), 529 (3), 599 (2), 621 (1), 659 (5), 694 (3), 778 (2), 812 (2), 853 (1), 1018 (2), 1044 (2), 1067 (2), 1180 (1), 1436 (2), 1457 (2), 2434 (2), 2439 (2), 2541 (2), 2735 (2), 2844 (4), 2891 (1), 2941 (5), 3009 (4).

II. $(C_2H_5O)_2P(S)SH$: 193 (3), 323 (1), 355 (3), 397 (1), 451 (1), 510 (5), 543 (3), 593 (1), 656 (1), 773 (3), 848 (2), 953 (1), 1016 (2), 1047 (1), 1101 (4), 1239 (3), 1392 (2), 1450 (4), 1475 (3), 2439 (2), 2492 (2), 2543 (2), 2727 (2), 2735 (3), 2872 (3), 2893 (3), 2932 (5), 2980 (3).

III. $(C_2H_5O)_3PS$: 205 (2), 328 (1), 503 (2), 612 (4), 665 (3), 702 (2), 1023 (3), 1100 (4), 1288 (3), 1453 (4), 2864 (1), 2893 (2), 2831 (4), 2976 (4).

IV. $(n\text{-}C_3H_7O)_2P(S)SH$: 148 (2), 193 (2), 292 (1), 355 (4), 438 (2), 459 (1), 495 (2), 520 (3), 547 (3), 662 (5), 743 (3), 797 (2), 882 (3), 909 (1), 103 (3), 1060 (2), 1101 (1), 1129 (2), 1152 (1), 1255 (1), 1280 (3), 1302 (2), 1343 (1), 1393 (1), 1437 (3), 1457 (4), 2438 (3), 2493 (3), 2549 (3), 2740 (2), 2879 (4), 2935 (4), 2974 (4), 3046 (2).

V. $(n\text{-}C_3H_7O)_2P(S)OH$: 140 (2), 279 (2), 397 (2), 437 (1), 461 (1), 624 (5), 742 (2), 881 (2), 1017 (1), 1261 (1), 1282 (2), 1303 (1), 1354 (1), 1403 (2), 1441 (5), 1459 (5), 2457 (1), 2495 (1), 2747 (2), 2876 (3), 2924 (3), 2959 (3), 3048 (3), 3125 (3).

VI. (iso-$C_3H_7O)_2P(S)OH$: 446 (1), 619 (5), 722 (1), 760 (1), 894 (2), 936 (1), 1065 (2), 1147 (2), 1191 (2), 1267 (2), 1353 (2), 1455 (5), 1873 (3), 2488 (1), 2925 (3), 2942 (3), 2985 (3), 3045 (5), 3126 (2).

VII. (iso-$C_4H_7O)_2P(S)SH$: 151 (2), 514 (3), 533 (1), 636 (3), 663 (1), 706 (1), 743 (1), 796 (1), 876 (2), 897 (2), 1054 (3), 1103 (3), 1302 (3), 1347 (1), 1453 (3), 2494 (3), 2871 (4), 2916 (5), 2933 (4), 2965 (4), 3045 (3), 3128 (3).

The Raman spectra of esters of dithio- and thiophosphoric acids are set forth in the table. The numbers in parens represent the intensities of the lines on a five-point scale (visual evaluation).

All of the compounds have a fairly strong line in the 598-662 cm^{-1} region, which corresponds to the frequencies of the P= S bond according to the literature. The slight shift of the characteristic frequency into the long-wave region is considerably smaller than has been reported in the literature. It is caused by groups of similar structure and composition linked to the phosphorus atom [7]. Noteworthy features are the frequencies in the 2489-2495 and 2541-2549 cm^{-1} regions exhibited by compounds containing the P(S)SH and P(S)OH groups. These frequencies are absent from the spectrum of $(RO)_2P = S$. They were not reported by other investigators [4, 6, 7] for compounds not containing the P(S)SH and P(S)OH groups. Organic compounds of phosphorus with a P = S bond do not exhibit frequencies close to the above-mentioned spectra regions in the absence of PSH groups. The S-H bond frequency of mercaptans lies in the 2489-2495 cm^{-1} region. The frequency that we observed must be assigned to the characteristic frequency of the S-H bond shifted into the long-wave region owing to linking of the S-H group with phosphorus. The lower intensity of the lines of compounds with P(S)OH compared with P(S)SH compounds can be accounted for by the lower concentration of molecules containing the S-H bond.

SUMMARY

1. The Raman spectra of the investigated O,O-dialkyldithiophosphoric and dialkylthiophosphoric acids contain the P = S bond frequency (in the 598-662 cm^{-1} region), but it is slightly shifted toward the long-wave region due to the constitutional similarity of the groups attached to the phosphorus atom.

2. O,O-Dialkyldithiophosphoric acids have a characteristic frequency in the 2489-2495 cm^{-1} region belonging to the S-H bond and located nearer to the short-wave region than the S-H bond of mercaptans.

3. The characteristic frequency of the S-H bond with weakened intensity is found in esters of thiophosphoric acid due to thiono–thiol tautomerism of the latter.

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SYNTHESIS OF SILICON-CONTAINING AROMATIC ACIDS AND AMINES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4058-4060, December, 1960
Original article submitted February 15, 1960

In this paper we report work on the synthesis of acids and amines of the type of $R_3Si(CH_2)_nC_6H_4COOH$ and $R_3Si(CH_2)_nC_6H_4NH_2$.

According to the literature, mono- and dicarboxylic acids of the type of $\equiv SiC_6H_4COOH$ and $>Si(C_6H_4COOH)_2$ are obtained by treatment with carbon dioxide of the corresponding Grignard reagents [1-8] or organolithium compounds [1], by oxidation of tolylsilanes [3, 7, 9, 10] or ethylphenylsilanes [11], and by hydrolysis of the corresponding nitriles with aqueous alkali [9]. Chlorobenzyltrimethylsilanes were converted to o-, m-, and p-trimethylsilylmethylbenzoic acids via the organolithium compounds [12].

We employed the organomagnesium method for preparation of p-trialkylsilylalkylbenzoic acids (Table 1).

$$p\text{-}R_3Si(CH_2)_nC_6H_4Br \xrightarrow{Mg} p\text{-}R_3Si(CH_2)_nC_6H_4MgBr \xrightarrow{CO_2} p\text{-}R_3Si(CH_2)_nC_6H_4COOH$$

The low yields of acids are evidently due to the poor reactivity of the respective organomagnesium compounds, which had been observed in other cases.

According to the literature, aromatic amines substituted in the ring with silicoalkyl groups can be synthesized by reduction of nitro compounds by hydrogen (tin and hydrochloric acid) [3] or by hydrogenation in presence of nickel [5, 14, 15], as well as by treatment of the corresponding benzamides with sodium hypochlorite solution [5]. The nitro derivatives (mixture of ortho-, meta-, and para-isomers) of aromatic silicohydrocarbons can be prepared by nitration of the silicohydrocarbons with nitric acid [13, 14, 16, 17] or copper nitrate [18].

p-Trimethylsilylnitrobenzene was synthesized by the action of conc. HNO_3 on p-bis(trimethylsilyl)benzene [9]. This route is extremely attractive since one isomer is formed. Unfortunately we were unable to extend it to other para-silicon-substituted trimethylsilylbenzenes. It was found that when silicohydrocarbons $p\text{-}R_3Si(CH_2)_n\text{-}C_6H_4Si(CH_3)_3$ are treated with nitric acid the latter are nearly quantitatively oxidized, and nitro derivatives $p\text{-}R_3Si(CH_2)_nC_6H_4NO$ are formed in a yield of 2-3%.

Trimethylsilylalkylanilines (Table 2) were synthesized by reduction of the corresponding nitro compounds with hydrogen over Raney nickel under pressure (yield ~ 90%) or at atmospheric pressure with hydrazine hydrate also in presence of Raney nickel (yields ~ 90%).

EXPERIMENTAL

1. p-Trialkylsilylalkylbenzoic acids. As an example we give details of the synthesis of p-triethylsilylmethylbenzoic acid. A Grignard reagent prepared from 30 g (0.108 mole) of p-triethylsilylmethylbromobenzene was poured onto finely pulverized solid CO_2 (15 g). After the appropriate treatment the ethereal layer was collected and left overnight in a refrigerator at 2-4°. The precipitated crystals were filtered and twice reprecipitated from ligroine. Evaporation of the ethereal layer gave a further small quantity of crystals. Yield 3.9 g (14.8%).

TABLE 1

Acids	Yield (%)	Melting point	Calculated (%)			Found (%)		
			C	H	Si	C	H	Si
p-$(CH_3)_3SiCH_2C_6H_4COOH$	25	178°*	—	—	—	—	—	—
p-$(CH_3)_3SiCH_2CH_2C_6H_4COOH$	19	170	63.89	8.10	12.62	63.19, 63.00	8.04, 8.25	12.76, 12.54
p-$(C_2H_5)_3SiCH_2C_6H_4COOH$	14.8	140	66.41	8.81	11.38	65.73, 65.99	8.66, 8.84	10.88, 10.91
p-$(C_2H_5)_3SiCH_2CH_2C_6H_4COOH$	20	120	68.00	9.06	10.62	67.46, 67.72	8.89, 8.98	9.96, 10.17

*Literature data [12]: m.p. 179°.

TABLE 2

Amine	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Calculated (%)			Found (%)		
				C	H	Si	C	H	Si
p-$(CH_3)_3SiCH_2C_6H_4NH_2$	90° (5)* M.p. 35°	—	—	—	—	—	—		
p-$(CH_3)_3Si(CH_2)_2C_6H_4NH_2$	103 (5)	1.5201	0.9303	68.15	9.84	14.50	67.73, 67.63	9.92, 9.76	14.55, 14.72
o-$(CH_3)_3Si(CH_2)_2C_6H_4NH_2$	91 (5)	1.5211	0.9343	68.15	9.84	14.50	67.84, 67.98	9.93, 10.04	14.83, 14.92
p-$(CH_3)_3Si(CH_2)_3C_6H_4NH_2$	110 (5)	1.5178	0.9257	69.61	10.18	13.52	69.68, 69.50	10.27, 10.36	13.35, 13.60
p-$(CH_3)_3Si(CH_2)_4C_6H_4NH_2$	121 (5)	1.5135	0.9206	70.52	10.44	12.60	69.78, 69.87	10.47, 10.34	12.03, 12.25

*Literature data [15]: b.p. 119°(10 mm); m.p 33.5-34°.

2. Trialkylsilylalkylanilines. a) Into a rotating steel autoclave (one-liter capacity) were charged 20 g of nitro compound, 50 ml of anhydrous ethanol, and 1-2 g of Raney nickel. Initial hydrogen pressure 70 atm. Working temperature 50°. The calculated quantity of hydrogen was absorbed in the course of 3-4 hr. After the catalyst had been separated, the trialkylsilylalkyl aniline was isolated by fractional distillation. Yield 85-90%.

b) In a round-necked flask fitted with reflux condenser were placed 20 g of nitro compound, 200 ml of ethanol, a threefold excess of aqueous hydrazine hydrate, and 1.5 g of Raney nickel. The mixture was heated at the boil on a water bath until complete decolorization of the solution (2-2.5 hr). After addition of another 1-2 g of Raney nickel, the mixture was heated for another 2-3 hr for decomposition of the excess of hydrazine hydrate. The catalyst was separated, the mixture was heated with active carbon, the filtrate diluted with water (500 ml), and the organic layer extracted with ether. The trialkylsilylalkylanilines were isolated by fractional distillation. Yield 80-90%.

SUMMARY

A series of trialkylsilylalkylbenzoic acids and trialkylsilylalkylanilines was synthesized.

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SYNTHESIS OF N-CHLOROPHOSPHAMIDES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4060-4064,
December, 1960
Original article submitted February 15, 1960

A large number of the most diverse N-chloroamides prepared on the basis of amides of sulfonic or carboxylic acids, as well as chloroamines, have been recently described. N-Chlorophosphamides were unknown before 1956. The literature contains a reference only to N-chloro-(β-chloroethyl)-amidodialkylphosphates, obtained by reaction of chlorine with dialkylethyleneamidophosphates [1].

The present work was undertaken with the objective of synthesizing various N-chlorophosphamides and of developing general methods for their preparation. The starting phosphamides were prepared by reaction of the amine with the appropriate acid chloride in ether or chloroform [2-4]. The properties of the starting phosphamides not described in the literature are set forth in Table 1.

Replacement of hydrogen atoms in the alkylamido group of the phosphamide by chlorine was effected by treatment of a chloroform solution of the phosphamide with excess of alkaline sodium hypochlorite solution.

Dichloroamides were prepared by chlorination of the phosphamide with chlorine gas in presence of sodium acetate or zinc oxide in carbon tetrachloride.

N-Chlorophosphamides were separated by extraction of the reaction mass with chloroform or carbon tetrachloride, drying of the extract, and thorough removal of solvent at room temperature in vacuo without subsequent distillation.

Diphenyl amidophosphate, insoluble in water and carbon tetrachloride, was subjected to chlorination with chlorine gas in a mixture of carbon tetrachloride and water (1: 2) in presence of excess of sodium acetate.

All of the prepared N-chlorophosphamides are yellowish liquids with a pungent odor, soluble in organic solvents. Some members are also soluble in water. A chloroform solution of an N-chlorophosphamide acts on an acetic acid solution of potassium iodide with quantitative liberation of iodine which titrates with thiosulfate. The content of active chlorine was determined by this procedure.

The least stable of the preparations were derivatives of methylphosphonic acid which decompose in the course of a few days with reduction in the content of active chlorine to 1-2%. The most stable member is diphenyl N-dichlorodimethylamidophosphate whose active chlorine content fell by 3% after storage for 30 days.

A mixture of the original diphenyl N-methylamidophosphate (m.p. 95°) [3] and the amide obtained by decomposition of diphenyl N-chloromethylamidophosphate by heating with alcohol in presence of hydrochloric acid did not exhibit a depression of melting point (95°).

The properties of the prepared N-chlorophosphamides are set forth in Table 2.

TABLE 1

Prep. No.	Formula	Boiling point (pressure in mm)	Melting point	d_4^{20}	n_D^{20}	Found		Calculated	
						% P	% N	% P	% N
1	$C_6H_5O-P(=O)(NHC_2H_5)(NHC_2H_5)$	179° (0.7)	—	1.1104	1.5152	13.9, 14.0	12.5, 12.7	13.60	12.30
2	$CH_3-P(=O)(OC_6H_5)(NH_2)$	—	98°	—	—	18.05, 17.93	8.10, 7.91	18.15	8.17
3	$CH_3-P(=O)(OC_6H_5)(NHCH_3)$	132 (0.2)	—	1.1600	1.5252	16.46, 16.51	—	16.75	—
4	$CH_3-P(=O)(OC_6H_5)(NHC_2H_5)$	142 (0.2)	—	1.1330	1.5169	15.35, 15.65	7.08, 7.04	16.42	6.97
5	$C_6H_5-P(=O)(OC_6H_5)(NH_2)$	—	127	—	—	13.61, 13.30	6.27, 6.27	13.30	6.03

EXPERIMENTAL*

N-Chlorophosphamides were prepared by one of the following methods.

1. a) In the course of 2 hr a ninefold excess of sodium hypochlorite was added with cooling and vigorous shaking to a solution of 6 g of diphenyl methylamidophosphate in 15 ml of carbon tetrachloride in a conical flask fitted with a ground-glass stopper. The organic layer was separated and dried over calcined sodium sulfate. The solvent was completely removed in the vacuum of a water jet pump at room temperature until the gauge recorded a constant pressure of 10-15 mm. The undistilled product was then analyzed and subjected to further tests. Yield 4.3 g (63.5%) of phenyl N-chloromethylamidophosphate. A yellowish liquid with a sharp odor soluble in organic solvents and insoluble in water; d^{20}_4 1.2894, $n^{20}D$ 1.5557.

Found %: Cl_{active} 23.40, 23.58; Cl 11.99, 12.04; P 10.24, 10.10. $C_{13}H_{13}O_3NPCl$. Calculated %: Cl_{active} 23.9; Cl 11.95; P 10.40.

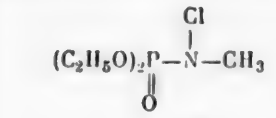
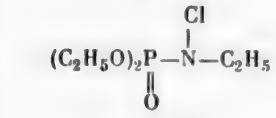
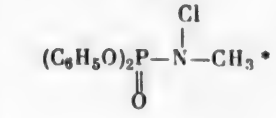
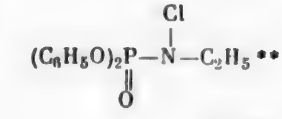
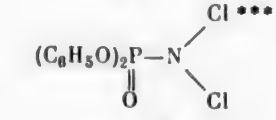
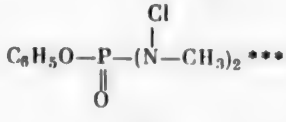
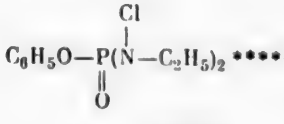
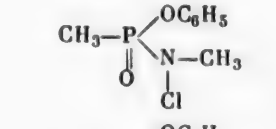
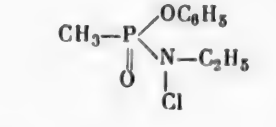
The hypochlorite solution was prepared by dissolving 32 g of dry sodium hydroxide in 130 ml of water and passing gaseous chlorine through the alkali solution, cooled with ice and salt, until the weight had increased by 27 g, so that after addition of potassium iodide and acetic acid 0.2 ml of the hypochlorite solution titrated with 10.2 ml of 0.1 N thiosulfate solution.

b) In the course of 2 hr a solution of 3 g of phenyl dimethyldiamidophosphate in 20 ml of chloroform was added slowly with stirring and cooling (to 2-3°) to 73 ml of freshly prepared sodium hypochlorite solution (0.18 g of active chlorine per milliliter). An additional 36 ml of sodium hypochlorite was then added and the mixture stirred for 30 min. The chloroform layer was separated, and the aqueous layer twice extracted with chloroform (5 ml each time). The chloroform solution was dried and the solvent taken off in vacuo to leave 3.7 g (92.5%) of phenyl N,N-dichlorodimethyldiamidophosphate; d^{20}_4 1.3688, $n^{20}D$ 1.5380. A yellowish liquid, easily soluble in organic solvents and insoluble in water.

Found %: Cl_{active} 52.40, 52.28; P 10.68, 10.56. $C_8H_{11}O_2N_2PCl_2$. Calculated %: Cl_{active} 52.8; P 10.40.

*V. I. Viryukin (1956), V. M. Grigor'ev (1957), and O. A. Pan'shin (1957) participated in the experimental work.

TABLE 2

Prep. No.	Formula	d_4^{20}	n_D^{20}	Active chlorine content (%) found	Active chlorine content (%) calc.	Solubility in organic solvents	Solubility in water	Yield (%)
1		1.2245	1.4380	35.2	35.4	+	+	60
2		1.2156	1.4390	32.8	33.0	+	+	80
3	 *	1.2994	1.5557	23.6	23.9	+	—	63
4	 **	1.2812	1.5470	22.6	22.8	+	—	70
5	 ***	1.5456	1.5603	44.3	44.6	+	—	85
6	 ****	1.3638	1.5380	52.3	52.8	+	—	92
7	 *****	1.2908	1.5230	47.3	47.8	+	—	91
8		1.2930	1.5270	32.2	32.3	+	+	52
9		1.2503	1.5230	30.2	30.4	+	+	50

*Found %: P 10.24, 10.10; Cl 12.04, 11.99. Calculated %: P 10.40, Cl 11.95.

**Found %: P 10.30, 10.24; Cl 12.31, 12.24. Calculated %: P 9.85; Cl 11.4.

***Found %: N 4.69, 4.56. Calculated %: N 4.40.

****Found %: N 10.68, 10.56. Calculated %: N 10.40.

*****Found %: N 9.71, 9.62. Calculated %: N 9.42.

c) Into a mixture of diphenyl amidophosphate, 20 ml of carbon tetrachloride, 40 ml of water, 6.7 g of sodium acetate, and 0.5 ml of glacial acetic acid with stirring at 2° was passed gaseous chlorine for 1.5 hr until the solid had dissolved completely. The organic layer was separated and the aqueous layer extracted. After drying, the solvent was distilled in vacuo. Yield 2.18 g (85%) of diphenyl N-dichlorodiamidophosphate: d^{20}_4 1.5456, $n^{20}D$ 1.5603.

Found %: Cl_{active} 44.3, 44.6; N 4.69, 4.56. $C_{12}H_{10}O_3NPCl_2$. Calculated %: Cl_{active} 44.65; N 4.40.

2. Decomposition of N-chlorophosphamides by alcohol. Diphenyl N-chloromethylamidophosphate (2 g) and absolute alcohol (50 ml) were stirred in presence of a drop of hydrochloric acid. Heat was liberated. The mixture was later refluxed for 10 min on a boiling water bath until a test for chlorine with starch-iodide paper was negative. Removal of the alcohol by distillation left 0.8 g of solid which after recrystallization from a mixture of benzene and ether melted at 95°. A mixture with the original diphenyl methylamidophosphate did not give a depression of melting point and likewise melted at 95° [3].

SUMMARY

Nine previously undescribed representatives of a new class of N-chlorophosphamides and five phosphamides were prepared.

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PREPARATION OF TETRAFLUORODIMETHYL DISELENIDES AND SOME OF THEIR PROPERTIES

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4064-4066, December, 1960
Original article submitted January 11, 1960

We established that tetrafluorodimethyl diselenide is obtained, analogously to hexafluorodimethyl diselenide [1], by decarboxylation of the mercury salt of difluoroacetic acid in presence of selenium.

$$(CF_3CO_2)_2Hg \xrightarrow{S} CF_3SeSeCF_3$$
$$(CHF_2CO_2)_2Hg \xrightarrow{Se} CHF_2SeSeCHF_2$$

Comparison of these reactions with the known reaction of salts of trifluoroacetic acid with sulfur [2] shows that decarboxylation of salts of fluorocarboxylic acids in presence of elements of Group 6 can proceed in two directions, depending on the location of the chalcogenide in the Periodic System.

$$RC(=O)OMe \xrightarrow{S} (RCO)_2O + SO_2$$
$$RC(=O)OMe \xrightarrow{Se} RSeSeR$$

where R is fluoralkyl

Even with further increase in the atomic number of the element, decomposition of the salts will evidently proceed by route (2). It may be suggested that reaction of tellerium with salts of fluorinated carboxylic acids will lead to fluorinated dialkyl ditellurides.

We reacted tetrafluorodimethyl diselenide with bromine and obtained difluoromethylselenium bromide.

$$CHF_2SeSeCHF_2 \xrightarrow{Br_2} 2CHF_2SeBr$$

The latter enters with facility into reaction with potassium cyanide to form difluoromethylselenium cyanide, and it adds on to ethylene with formation of difluoromethyl-β-bromoethyl selenide.

$$CHF_2SeBr \xrightarrow{KCN} CHF_2SeCN$$
$$CHF_2SeBr \xrightarrow{CH_2=CH_2} CHF_2SeCH_2CH_2Br$$

EXPERIMENTAL

We prepared difluoroacetic acid by hydrolysis of the product of interaction of diethylamine with tetrafluoroethylene [3].

Tetrafluorodimethyl diselenide. Colloidal selenium (24 g), well-dried over phosphorus pentoxide, and difluoroacetate (19.5 g) were mixed and placed in a glass tube about 20 mm in diameter and 200 mm in length, sealed at one end. The reaction mixture was gradually heated over a bare flame and the reaction products collected in a trap cooled with liquid air. (Inadequate cooling of the receiver results in entrainment of a considerable part of the diselenide with the carbon dioxide evolved during the process.) After completion of the reaction,

the content of the trap was slowly heated to room temperature. The resulting liquid was washed with an equal volume of ice water, dried with sodium sulfate, and distilled. Yield of tetrafluorodimethyl diselenide 2.4 g (26.5%). A yellowish liquid, readily soluble in acetone, alcohol, and ether, insoluble in water.

B.p. 118°, $n^{20}D$ 1.4910, d^{20}_4 2.280.

Found %: C 9.77; H 1.12; Se 60.44; F 29.66. $C_2H_2Se_2F_4$. Calculated %: C 9.24; H 0.77; Se 60.75; F 29.23.

Difluoromethylselenium bromide. Bromine (3.2 g) was gradually added dropwise to tetrafluorodimethyl diselenide (5.2 g) cooled with ice water. The reaction is slightly exothermic. With increasing accumulation of difluoromethylselenium bromide the liquid turned pink and then dark-red. The liquid was distilled 15 min after the calculated quantity of bromine had been added. Yield of difluoromethylselenium bromide 7.5 g (88%). A dark-red liquid, readily soluble in ether, hydrolyzed by water.

B.p. 94°, $n^{20}D$ 1.5082, d^{20}_4 2.4480.

Found %: Se 37.26; F 18.58; Br 38.36. $CHSeF_2Br$. Calculated %: Se 37.62; F 18.10; Br 38.07.

Difluoromethylselenocyanide. To a solution of 4.2 g of difluoromethylselenium bromide in 16 ml of ether was added in small portions a solution of 1.4 g potassium cyanide in 2 ml of water with stirring. Slight heat was liberated during the reaction. Potassium bromide crystals came down and the color of the solution changed from dark-red to light-yellow. After completion of the reaction, the liquid was separated, dried with sodium sulfate, and fractionated. Yield of difluoromethylselenocyanide 2.8 g (88%). A light-yellow liquid, readily soluble in common organic solvents, insoluble in water.

B.p. 128°, $n^{20}D$ 1.4525, d^{20}_4 1.8267.

Found %: N 8.73; Se 50.49; F 24.51. C_2HNSeF_2. Calculated %: N 8.98; Se 50.64; F 24.36.

Difluoromethyl-β-bromoethyl selenide. Into a test tube, fitted with inlet and outlet tubes, was charged 2.8 g of difluoromethylselenium bromide. The inlet tube was connected to a gasholder filled with ethylene. Dry ethylene was blown through the test tube until complete removal of air, and then the exit tube was cooled. The calculated quantity of ethylene was taken up after several hours. The reaction mass gradually became paler, and at the end of the process it was light-yellow. The resulting liquid was distilled at reduced pressure. Yield of difluoromethyl-β-bromoethyl selenide nearly quantitative. A light-yellow liquid, readily soluble in common organic solvents, insoluble in water.

B.p. 57° (6 mm), $n^{20}D$ 1.5421, d^{20}_4 2.0956.

Found %: Se 33.26; F 16.50; Br 33.44. $C_3H_5SeF_2Br$. Calculated %: Se 33.18; F 15.97; Br 33.58.

SUMMARY

Methods of preparation of new fluorinated organic compounds are described: symmetrical tetrafluorodimethyl diselenide, difluoromethylselenium bromide, difluoromethylselenocyanide, and difluoromethyl-β-bromoethylselenium bromide.

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METHODS OF PREPARATION OF FLUORO ANALOGS OF DICHLOROFORMOXIME

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4066-4069,
December, 1960
Original article submitted January 11, 1960

In preceding work it was shown that some fluorinated alkylsulfenyl halides can be utilized as starting substances for the synthesis of diverse fluorinated organic compounds [1-3].

The present investigation was undertaken with the objective of ascertaining the possibility of preparation of fluoro analogs of dichloroformoxime by nitrosation and reduction of fluoro analogs of trichloromethylsulfenyl chloride.

We know that dichloroformoxime can be prepared by reaction of trichloronitrosomethane with hydrogen sulfide [4].

$$CCl_3NO \xrightarrow{H_2S} CCl_2NOH + HCl + S$$

It was conceivable that fluorodichloronitrosomethane would behave like trichloronitrosomethane and would be reduced by hydrogen sulfide to fluorochloroformoxime. This expectation was confirmed. Reaction of fluorodichloronitrosomethane with hydrogen sulfide in ethereal solution leads to quantitative precipitation of sulfur, and hydrogen chloride is evolved.

$$CFCl_2NO \xrightarrow{H_2S} CFClNOH + HCl + S$$

After a small quantity of ether had gone off from the reaction mass with gaseous products, the fluorochloroformoxime distilled with the main bulk of ether. The Cl : F : N ratio in all fractions of the ethereal solution was 1 : 1 : 1, whereas in the starting substance the Cl : F : N ratio was 2 : 1 : 1.

The fluorochloroformoxime could not be separated from the ether by distillation. Colorless crystals came down when concentrated solutions of fluorochloroformoxime were allowed to stand. The analysis corresponded to fluorochloroformoxime, but the product was a polymer.

Attempts to extend these experiments to difluorochloronitrosomethane showed that in ethereal solution the reaction with hydrogen sulfide is also accompanied by separation of sulfur and evolution of hydrogen chloride; in no instance, however, were the ethereal solutions found to contain exactly one atom of nitrogen to two atoms of fluorine.

Precipitation of sulfur, evolution of hydrogen chloride, absence of chlorine, and presence of fluorine and nitrogen in the last fractions of ethereal solution evidently indicated the formation of the very unstable difluoroformoxime.

Trihalonitrosomethanes were obtained by reaction of fluoro analogs of trichloromethylsulfenyl chloride [5] with nitric acid.

EXPERIMENTAL

Fluorodichloronitrosomethane and fluorodichloromethane sulfochloride. In a round-bottomed, 250 ml flask, fitted with stirrer, mercury seal, and side tube, were placed 16.95 g of fluorodichloromethylsulfenyl chloride [5] and 85 ml of 33% nitric acid. The flask was immersed in a water bath at room temperature and the mixture vigorously stirred for 4 hr. During the reaction the bath temperature was not allowed to rise above 20-24°. Gases were collected in a trap cooled with acetone and solid carbon dioxide. The exit tube of the trap was connected to a sulfuric acid wash bottle.

After the reaction had finished, the content of the trap was slowly heated to 0° and quickly washed with a small quantity of ice water while air was blown through the trap in order to oxidize the nitric oxide to dioxide. The resulting blue oil was separated from the water, dried with calcium chloride, and distilled at 11 to 14°. The main fraction of fluorodichloronitrosomethane distilled at 12°. Yield 1.1 g (8.3%).

Found %: C 8.95; N 10.37; F 14.90; Cl 53.17; NO 22.52. $CONFCl_2$. Calculated %: C 9.09; N 10.6; F 14.4; Cl 53.78; NO 22.72.

During the reaction with nitric acid, fluorodichloromethane sulfochloride was formed in addition to fluorodichloronitrosomethane. This compound remains in the reaction flask in the form of a solid, blue mass. It was left to stand at room temperature for several days. The solid was then separated from the nitric acid and the fluorodichloromethane sulfochloride distilled with steam and dried in a desiccator over calcium chloride. Yield of fluorodichloromethane sulfochloride 6.2 g (26%). Colorless crystals with m.p. 56° and b.p. 124° (with partial decomp.).

Found %: C 5.83; S 16.06; F 9.13; Cl 52.32. CO_2SFCl_3. Calculated %: C 5.97; S 15.92; F 9.45; Cl 52.23.

Difluorochloronitrosomethane and difluorochloromethane sulfochloride. In a 250 ml round-bottomed flask, fitted with stirrer, mercury seal, and side tube, were placed 22.6 g of difluorochloromethylsulfenyl chloride [5] and 115 ml of 33% nitric acid. The flask was immersed in an ice water bath and the mixture stirred vigorously for 30 min. The bath was then heated to 20-30° and vigorous stirring continued. Gases were collected in a trap cooled with a mixture of acetone and solid carbon dioxide. The exit tube of the trap was connected to a sulfuric acid wash bottle. Stirring was stopped after 3 hr, the content of the trap was distilled into a gasholder filled with water, and with vigorous agitation the gases in the gasholder were mixed with air until the nitric oxide had been completely oxidized to dioxide and the nitrogen dioxide had dissolved in the water. The blue-colored gas, free of oxides of nitrogen, was passed through a calcium chloride tube and fractionated in a column suitable for volatile substances. The main fraction, boiling at −36 to −28°, had the empirical composition and molecular weight of a mixture of difluorochloronitrosomethane and difluorodichloromethane. In the pure form difluorochloronitrosomethane distils at −36°. The literature [6] gives the same boiling point. Total yield of difluorochloronitrosomethane 1.78 g (10.3%).

Found %: F 33.07; Cl 30.63. $CONF_2Cl$. Calculated %: F 32.9; Cl 30.73.

Reaction of difluorochloromethylsulfenyl chloride with nitric acid gave, apart from gaseous substances, difluorochloromethane sulfochloride. This compound remains in the reaction flask as a green oil. The reaction mass was allowed to stand for several days at room temperature. The oil was then separated from the nitric acid, distilled with steam, and dried with calcium chloride. Yield of difluorochloromethane sulfochloride 4.2 g (12.3%). A colorless liquid with b.p. 84.5° (with partial decomp.), $n^{17}D$ 1.4005, d^{17}_4 1.6763.

Found %: C 6.51; S 17.58; F 20.24; Cl 38.22. $CO_2SF_2Cl_2$. Calculated %: C 6.45; S 17.35; F 20.53; Cl 38.37.

Fluorochloroformoxime. In a 30 ml glass ampoule were placed 10 ml of well-dried ethyl ether and 4 g of freshly prepared fluorodichloronitrosomethane. After solution of the nitroso compound, 1.3 g of hydrogen sulfide (dried with calcium chloride) was added. The ampoule was then sealed, energetically shaken several times, and left overnight at room temperature. The mass became colorless during the reaction in the ampoule and sulfur was quantitatively precipitated. The next day the ampoule was opened and held at room temperature for about 30 min, until hydrogen chloride ceased to be evolved. The ethereal solution was then decanted and transferred to a distillation apparatus while excess of air was rigorously excluded. Distillation was performed at room temperature and reduced pressure. The products were collected in a receiver cooled with liquid nitrogen. The first

fractions were gaseous impurities and a considerable proportion of the ether together with a small amount of fluorochloroformoxime. The main bulk of the fluorochloroformoxime came over with the last portions of ether. If, for example, about 3 g of ethereal solution had remained in the distillation flask, continuation of distillation gave a 1st fraction with a 45.3% content of fluorochloroformoxime and a 2nd fraction with 54.2% content of fluorochloroformoxime. Further concentration of the 2nd fraction yielded about 0.5 g of ethereal solution with a 70% content of fluorochloroformoxime.

After the concentrated ethereal solution of fluorochloroformoxime had been kept for a few days, it deposited a minute quantity of colorless crystals corresponding in analysis to the polymer of fluorochloroformoxime. The crystals decomposed when heated.

Found %: N 14.47; F 19.57; Cl 36.57. $(CHONFCl)_n$. Calculated %: N 14.35; F 19.48; Cl 36.41.

SUMMARY

1. Reaction of fluorodichloromethylsulfenyl chloride and difluorochloromethylsulfenyl chloride with nitric acid gives the corresponding nitroso compounds and sulfochlorides.

2. It was shown that reaction of fluorodichloronitrosomethane with hydrogen sulfide gives fluorochloroformoxime (in ethereal solution).

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PREPARATION OF HALOGENATED DIALKYL DISELENIDES AND SYMMETRICAL TETRAFLUORODICHLORODIMETHYL DISULFIDE

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4069-4071,
December, 1960
Original article submitted January 28, 1960

Halogenated dialkyl diselenides are starting substances for preparation of alkylselenium halides, which in turn are starting products for synthesis of diverse halogenated, selenium-containing organic compounds. According to the literature, halogenated dialkyl diselenides are formed in admixture with other compounds when fluorinated organic compounds are reacted with selenium [1, 2]; they are also obtained by chlorination of selenoformaldehyde in an inert solvent [3]. We recently showed that fluorinated dialkyl diselenides can also be obtained by decarboxylation of fluorocarboxylic acids in presence of elemental selenium [4, 5].

In the present work we found that fluorinated dialkyl diselenides can also be obtained by reaction of selenium monobromide with tetrafluoroethylene.

$$Se_2Br_2 + CF_2{=}CF_2 \longrightarrow \begin{matrix} SeCF_2CF_2Br \\ | \\ SeCF_2CF_2Br \end{matrix}$$

This reaction is very sensitive to temperature and duration of heating. The best yield of diselenide is obtained by gradual heating of the starting components in an inert solvent to 160°. The initially formed diselenide is brominated by the selenium bromide if the reaction mixture is heated quickly to a high temperature, and considerable amounts of elemental selenium then separate out.

The structure of the resulting diselenide was verified by chlorination to 2-bromo-1,1,2,2-tetrafluoroethylselenium chloride:

$$\begin{matrix} SeCF_2CF_2Br \\ | \\ SeCF_2CF_2Br \end{matrix} \xrightarrow{Cl_2} BrCF_2CF_2SeCl$$

Some halogenated alkylselenium halides, also alkylsulfenyl halides, can be reduced to halogenated dialkyl diselenides or dialkyl disulfides respectively:

$$CF_3SeCl \xrightarrow{Sn} CF_3SeSeCF_3$$

$$CF_2ClSCl \xrightarrow{KI} CF_2ClSSCF_2Cl$$

It is known that reaction of selenium monochloride with ethylene does not lead to 2,2'-dichlorodiethyl diselenide; in this case the reaction goes according to the equation [6]:

$$Se_2Cl_2 + CH_2{=}CH_2 \longrightarrow (ClCH_2CH_2)_2SeCl_2 + Se$$

2,2'-Dichlorodiethyl diselenide, as we have shown, can be prepared by reaction of 2,2'-dihydroxydiethyl diselenide with concentrated hydrochloric acid.

$$(HOCH_2CH_2Se{-})_2 \xrightarrow{HCl} (ClCH_2CH_2Se{-})_2$$

The 2,2'-dihydroxydiethyl diselenide required for this reaction was prepared together with 2-hydroxyethylselenomercaptan by reaction of ethylene oxide with hydrogen selenide under pressure.

$$\underset{\diagdown\,O\,\diagup}{CH_2{-}CH_2} + H_2Se \longrightarrow HOCH_2CH_2SeH \xrightarrow{O_2} (HOCH_2CH_2Se{-})_2$$

The intermediate product – 2-hydroxyethylselenomercaptan – is very easily oxidized to the diselenide. Hence if addition of hydrogen selenide to ethylene oxide is performed in presence of air, the product of oxidation (the diselenide) is formed simultaneously.

Up to now the reaction of hydrogen selenide with organic α-oxides has been carried out only in the acetylenic and vinylacetylenic α-oxide series for the preparation of selenophenes without isolation of the intermediate products – the selenomercaptans [7].

Halogenated dialkyl diselenides are colored liquids with an unpleasant odor, insoluble in water.

EXPERIMENTAL

Preparation of 2,2'-dibromo-1,1,1',1',2,2,2',2'-octafluorodiethyl diselenide. A solution of 9.0 g (0.028 mole) of selenium monobromide in 60 ml of carbon tetrachloride and 6.7 g (0.067 mole) of tetrafluoroethylene were placed in a glass tube of 150 ml capacity. The tube was then sealed and heated on an oil bath for 4-5 hr (1 hr at 110°, 2-3 hr at 140°, and 1 hr at 160°). After cooling, the tube was opened, gaseous products and solvent were distilled off, and the residue washed several times with small portions of hot water. The brown-red liquid product was dried with sodium sulfate and distilled Yield 1.6 g (11%).

B.p. 75° (5 mm), $n^{18}D$ 1.4818, d^{18}_4 2.5279.

Found %: C 8.83; Se 31.19; F 29.42; Br 30.87. $C_4Se_2F_8Br_2$. Calculated %: C 9.25; Se 30.50; F 29.34; Br 30.91.

Preparation of 2-bromo-1,1,2,2-tetrafluoroethylselenium chloride. Chlorine was passed at −10 to −15° through 6.0 g of 2,2'-dibromooctafluorodiethyl diselenide until the weight had increased by 0.87 g. The reaction mixture was then decomposed at atmospheric pressure. Yield of 2-bromotetrafluoroethylselenium chloride 3.75 g (55%).

B.p. 121°, $n^{16}D$ 1.4578, d^{16}_4 2.3436.

Found %: C 8.50; Se 26.71; F 25.82; Cl 12.18; Br 27.08. C_2SeF_4ClBr. Calculated %: C 8.15; Se 26.83; F 25.81; Cl 12.05; Br 27.16.

Reaction of trifluoromethylselenium chloride with tin. In a three-necked flask fitted with dropping funnel, reflux condenser, and thermometer were put 2.5 g of tin and 5 ml of hydrochloric acid, followed dropwise by 36 g of trifluoromethylselenium chloride [4]. The reaction is exothermic. After cooling of the reaction mixture to room temperature, the oil was separated, dried with calcium chloride, and distilled. Yield of hexafluorodimethyl diselenide nearly quantitative.

B.p. 70°, $n^{18}D$ 1.4038, d^{18}_4 2.2030 (b.p. 70°, $n^{18}D$ 1.4035 [4]).

Found %: F 38.87. $C_2Se_2F_4$. Calculated %: F 38.51.

Reaction of difluorochloromethylsulfenyl chloride with potassium iodide. A solution of 15.3 g of difluorochloromethylsulfenyl chloride [8] in 60 ml of ether was run in small portions, with ice water cooling and stirring, into a solution of 13.3 g of potassium iodide in 12 ml of water. The reaction mixture was allowed to stand for 30 min; the ether layer was separated, the iodine decolorized with thiosulfate solution, and the liquid dried with sodium sulfate and distilled. Yield of symmetrical tetrafluorodichlorodimethyl disulfide 6.2 g (55%).

B.p. 62° (95 mm), d^{19}_4 1.5270, $n^{19}D$ 1.4345.

Found %: C 10.27; S 27.54; F 32.19; Cl 29.83. $C_2S_2F_4Cl_2$. Calculated %: C 10.21; S 27.24; F 32.34; Cl 30.21.

Preparation of 2-hydroxyethylselenomercaptan and 2,2'-dihydroxydiethyl diselenide. A mixture of 2.2 g (0.05 mole) of ethylene oxide and 7.5 g (0.091 mole) of hydrogen selenide was sealed into a 250 ml glass ampoule which was then placed in a water bath at room temperature and allowed to stand for 100 hr. The liquid acquired a lemon-yellow color. The ampoule was opened, the excess of hydrogen selenide distilled off, and the residual liquid fractionally distilled.

The first fraction (b.p. 75° at 16 mm) was 2-hydroxyethylselenomercaptan. Yield 2.4 g.

$n^{20}D$ 1.5380, d^{20}_4 1.5890.

Found %: C 19.44; H 4.24; Se 63.18. C_2H_6OSe. Calculated %: C 19.21; H 4.80; Se 63.18.

The second fraction (b.p. 185° at 5 mm) was 2,2'-dihydroxydiethyl diselenide. Yield 1.5 g.

Found %: C 19.31; H 4.71; Se 62.55. $C_4H_{10}O_2Se_2$. Calculated %: C 19.38; H 4.04; Se 63.78.

Preparation of 2,2'-dichlorodiethyl diselenide. To 2.0 g of 2,2'-dihydroxydiethyl diselenide was added 6.0 ml of concentrated hydrochloric acid. After 30 min standing, the diselenide formed an emulsion from which an orange oil separated. The latter was washed with water and dried with sodium sulfate. Yield 1.8 g (78%). Decomposes on distillation.

$n^{20}D$ 1.6512, d^{20}_4 1.8850.

Found %: Se 55.19; Cl 24.46. $C_4H_8Se_2Cl_2$. Calculated %: Se 55.46; Cl 24.89.

SUMMARY

1. For the first time the addition of selenium halides to tetrafluoroethylene was carried out, and 2,2'-dibromooctafluorodiethyl diselenide was prepared.

2. Addition of hydrogen selenide to ethylene oxide was effected for the first time, and from the reaction products were isolated 2-hydroxyethylselenomercaptan and 2,2'-dihydroxydiethyl diselenide.

3. A method of preparation of symmetrical tetrafluorodichlorodimethyl disulfide was described.

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SYNTHESIS OF o-AMINOBENZENEPHOSPHONIC ACID AND ITS DERIVATIVES*

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4072-4076, December, 1960
Original article submitted January 3, 1960

According to the literature the synthesis of o-aminobenzenephosphonic acid (o-$NH_2C_6H_4PO_3H_2$) has been effected only by one method—replacement of the bromine in o-bromobenzenephosphonic acid by the amino group [2]. Out attempts to repeat this synthesis gave unsatisfactory results. The reaction appears to go in two directions: 1) the bromine in o-bromobenzenephosphonic acid is replaced by the hydroxy group to give o-hydroxybenzenephosphonic acid (40%); 2) bromine is replaced by the amino group, but at the instant of formation of o-aminobenzenephosphonic acid the C-P bond undergoes hydrolysis with formation of aniline (15%). Similar examples of rupture of a C-P bond during synthesis of benzenephosphonic acids were reported by a number of authors [3-5].

By analogy with the meta- and para-isomers [6-8], a possible route to o-aminobenzenephosphonic acid would appear to be reduction of o-nitrobenzenephosphonic acid. But the latter is obtained in a yield of only 5-6% by nitration of benzenephosphonic acid, and the conditions of isolation are complex. We therefore decided not to pursue this method and turned our attention instead to the method of synthesis from o-nitroaniline proposed by Doak and Freedman [10]. However, no trace could be detected, under any conditions of performance of the reaction, of any nitro compound, apart from o-nitrophenol, reported in the literature [2, 5, 10]. At the same time, on thorough examination of the mother liquor which we suspected to contain o-nitrobenzenephosphonic acid, we completely unexpectedly found a compound capable of diazotization. By coupling with 1-naphthol-4-sulfonic acid we were able to isolate the corresponding amine in the form of an azo dye. Investigation of this azo compound showed that it was a mixture of two azo dyes. One of these was the product of coupling of chloroaniline, and the other of an amine containing chlorine and a phosphonic grouping. Further investigation established (see Experimental) that the second amine is 2-amino-5-chlorobenzenephosphonic acid (I).

With the objective of preparing amine (I) itself directly, we investigated a method of isolating it in the form of complexes** with heavy metals. We reasoned that the presence of a phosphonic group in the ortho-position to the amino group should intensify the complexing ability of (I) relative to chloroaniline, and should consequently facilitate their separation. Separation could indeed be achieved through the copper complex; after decomposition of the latter the acid could be isolated in the chemically pure state. In this connection it was found necessary to increase the quantity of cuprous chloride severalfold over the amount recommended in [10], and also to modify the procedure for bringing it into reaction. It was likewise established that an increase in the quantity of PCl_3 by a factor of 3.5 gives optimum results and enables isolation of (I) in a yield of up to 15% (5% in the form of dye). All the remaining reaction conditions are found in the example described below.

*Communication III in the series on "Investigations in the field of arylphosphonic acids." For Communication II see [1].

**For simplicity of exposition we shall imply by the term "complexes" the corresponding products of interaction with cations with the investigation of whose structure we did not occupy ourselves.

In conclusion we must draw attention to the presence in the reaction mass of a series of substances in addition to (I), chloroaniline, and o-nitrophenol. Only after elucidation of the composition and structure of the latter shall we be able to more fully understand the mechanism of interaction of PCl_3 with the diazo compound from o-nitroaniline. But even at this stage we can say that the process is extremely complicated and comprises a series of interlinked reactions, three of which are responsible for the formation of the acid in which we are interested, namely: 1) replacement of the diazo group by the phosphonic group; 2) reduction of the nitro group; 3) chlorination.

From (I) we prepared six azo compounds, the coupling components being respectively R salt, chromotropic acid, H acid, 1-hydroxynphthalene-4-sulfonic acid, β-naphthol, and resorcinol. All of the prepared azo compounds contain the ring-forming grouping (II), analogous to the well-known grouping (III) which is present in components already widely employed in analytical practice [11-19].

(II) (III)

This analogy will naturally arouse interest in the analytical properties of the azo compounds now prepared. Results of their investigation and of a comparison with their arsonic analogs will be presented in a separate communication.

EXPERIMENTAL*

Reaction of o-bromobenzenephosphonic acid with ammonia [2]. The phosphonic acid was prepared essentially by the method of [20]. To a solution of 12 g of o-bromobenzenephosphonic acid (m.p. 199.5-201.5°) in 200 ml of ammonia solution (d 0.9) was added 9 g of freshly prepared cuprous oxide, and the mass was heated at 70-80° for 18 hr. It was then acidified with concentrated hydrochloric acid. The copper was brought down with hydrogen sulfide, the copper sulfide filtered off, and the mother liquor boiled with carbon. After filtration, the filtrate was divided into two equal parts. The first half was evaporated to 5 ml and cooled; the ammonium chloride was filtered off and the mother liquor evaporated to dryness. The residue was dried in vacuo over calcium chloride and then boiled with 50 ml of absolute alcohol. A considerable amount of material did not dissolve in the alcohol and consisted of a mixture of inorganic compounds. After filtration, the filtrate was cooled, but no precipitate came down, as had been expected according to [2]. A syrupy mass remained after the alcohol had been distilled. In alkali solution the syrup formed with the diazonium chloride from p-nitroaniline an azo dye containing phosphorus and agreeing in analysis with the product of coupling of diazo-p-nitroaniline with o-hydroxybenzenephosphonic acid (see [1]).

The second half of the solution was diazotized and coupled with β-naphthol. The resulting azo dye was twice reprecipitated by acidification of the carbonate solutions, and washed with water. There was obtained 0.8 g of orange substance. Sodium and phosphorus were absent.

Found %: C 77.47, 77.70; H 5.47, 5.28; N 11.01, 10.99. $C_{16}H_{12}ON_2$. Calculated %: C 77.39; H 4.85; N 11.28.

Preparation of 2-amino-5-chlorobenzenephosphonic acid (I). A solution of 80 g of o-nitroaniline was prepared by heating at 50° in 800 ml of hydrofluoboric acid (d 1.24); the solution was cooled to 3° and diazotized with vigorous stirring at + 3 to +8° by means of 40 g of sodium nitrite. Light-yellow crystals started to come down while the sodium nitrite was being added. After the whole of the nitrite had been added, the mass was kept for half an hour at −1°. The solid was filtered, washed with ice water (~ 50 ml), then with ethyl ether (~ 50 ml), and dried in the air to constant weight. Yield 118.5 g of o-nitroaniline diazonium fluoborate.

To a mixture of 635 ml of absolute ethyl acetate, 155 ml (1.75 moles) of phosphorus trichloride, and 25 g of cuprous chloride at 30° was added portionwise a mixture of 118.5 g (0.5 mole) of o-nitroaniline diazonium fluoborate and 25 g of cuprous chloride. The temperature rose during the addition, and at 50° nitrogen started to

*With participation of G. P. Stepanova.

come off. After the whole of the fluoroborate had been added, the temperature of the reaction mass was gradually raised to 65° in step with the progressive decrease of nitrogen evolution, and the mass was held at 65° for 3 hr. The next day 10 ml of water was added to the reaction mass at 15-35°, and the mass was reheated to 50-65° for an hour. Subsequently, with the temperature held at 45-60°, 590 ml of water was added, and the reaction mass was neutralized with sodium carbonate to pH 3 (using universal indicator paper) and heated to 45°. After cooling, the precipitated copper complex was filtered off. An additional crop of complex was isolated from the aqueous layer of the filtrate after addition of ethyl acetate. The precipitates were combined, washed with water, and dried at 100°. Yield 32 g of greenish substance. It was dissolved in dilute hydrochloric acid (1 : 2). The copper was brought down with hydrogen sulfide, the copper sulfide was filtered, and carbon added to the filtrate. The filtrate + the carbon was evaporated to $\frac{1}{2}$ its volume, the carbon was filtered off, and the mother liquor neutralized with sodium carbonate to pH 3. A white amorphous precipitate was formed and was filtered, washed with about 75 ml of ice water, and dried at 120°. Yield 11 g (10%) of white, amorphous substance Analysis for sodium [21] gave a negative result.

Found %: P 15.02, 14.97; Cl 17.04, 17.02; N 7.01, 7.08. $C_6H_7O_3NPCl$. Calculated %: P 14.91; Cl 17.09; N 6.75.

An additional quantity of 2-amino-5-chlorobenzenephosphonic acid was isolated from the mother liquor as the azo dye with resorcinol in the amount of 7.3 g (5% of the amine yield).

2-Amino-5-chlorobenzenephosphonic acid (I) is soluble in water and alcohol; it crystallizes from dilute hydrochloric acid and acidified alcohol in the form of well-formed, fine needles.

The structure of (I) was established by comparison of the hydroxychlorobenzenephosphonic acid prepared from (I) with the 2-hydroxy-5-chlorobenzenephosphonic acid isolated from its potassium salt [1]. To a suspension of 2.07 g in 20 ml of water and 3 ml of concentrated hydrochloric acid was added a solution of 0.8 g of sodium nitrite in 5 ml of water at 0 to +5°. During the addition of the nitrite the solid went into solution. The resulting solution was filtered and heated for an hour at 50-60°, during which operation nitrogen came off in a vigorous stream. The reaction mass was then heated to 90°, 2 ml of concentrated hydrochloric acid and 0.5 g of carbon were added, the mass was evaporated to about half its volume, and the carbon was filtered off. The cooled filtrate deposited crystals which were filtered, washed with water, and dried at 100°. Yield 0.8 g with m.p. 151.5°.

Found %: P 14.87, 14.65; Cl 17.47, 17.21; Na none. $C_6H_6O_4PCl$. Calculated %: P 14.86; Cl 17.00.

A solution of 1.5 g of the potassium salt of 2-hydroxy-5-chlorobenzenephosphonic acid [1] in 15 ml of concentrated hydrochloric acid was filtered and evaporated to dryness. The residue was dried at 100° and then in a vacuum-desiccator over caustic alkali. The 2-hydroxy-5-chlorobenzenephosphonic acid was then extracted with absolute ether. Yield 0.3 g of substance with m.p. 151°.

Found %: P 15.12, 15.10; Cl 16.75, 16.64; K none.

No appreciable depression of melting point occurred in a test with a mixture of the two substances.

Synthesis of azo dyes* from 2-amino-5-chlorobenzenephosphonic acid (I). a) A diazo solution prepared from 2.07 g of amine was added to a solution of 1.2 g of resorcinol in 40 ml of 10% Na_2CO_3. The resulting dye was isolated by acidification with concentrated HCl and recrystallized from weak hydrochloric acid before being dried at 80°. There was obtained 2.3 g of dark-red solid. λ_{max} 385 mμ (aqueous solutions for all the dyes).

Found %: P 9.35, 9.24; N 8.31, 8.20; Cl 10.52; Na none. $C_{12}H_{10}O_5N_2PCl$. Calculated %: P 9.42; N 8.53; Cl 10.79.

b) A diazo solution prepared from 2.07 g of amine was coupled with 2.7 g of 1-naphthol-4-sulfonic acid in sodium carbonate solution as described. There was obtained 2.1 g of reddish-orange solid. λ_{max} 500 mμ.

Found %: P 7.19, 6.83; Cl 7.91, 8.13; Na none. $C_{16}H_{12}O_7N_2SPCl$. Calculated %: P 7.00; Cl 8.01.

c) A diazo solution prepared from 2.07 g of amine was coupled with 3.6 g of R salt in sodium carbonate solution. The resulting azo dye was isolated by acidification with hydrochloric acid. Two reprecipitations from water by hydrochloric acid gave 2.5 g of bright-red azo dye in the form of the monosodium salt. λ_{max} 495 mμ.

*All of the azo dyes were dried at 160° before analysis.

Found %: P 5.66, 5.78; S 11.69, 11.8; Na 4.55, 4.17. $C_{16}H_{11}O_{10}N_2S_2PClNa$. Calculated %: P 5.68; S 11.77; Na 4.22.

d) A diazo solution prepared from 2.07 g of amine was coupled in sodium carbonate solution with 4 g of H acid. The azo dye was isolated by acidification with hydrochloric acid. Reprecipitation from water by hydrochloric acid gave 2.5 g of dark-red substance. λ_{max} 530 mμ.

Found %: P 5.49, 6.11; Cl 6.73, 6.46; S 11.54; Na none. $C_{16}H_{13}O_{10}N_3S_2PCl$. Calculated %: P 5.76; Cl 6.59; S 11.92.

e) The diazo solution prepared from 2.07 g of amine was coupled in a sodium hydroxide medium with 1.6 g of β-naphthol. The azo dye was isolated by acidification with hydrochloric acid, reprecipitated from sodium carbonate solution by hydrochloric acid, filtered, and washed with water until free of chlorine ion. Yield 2.2 g of orange substance. λ_{max} 490 mμ.

Found %: P 8.78, 8.98; N 7.82, 7.53; Na none. $C_{16}H_{12}O_4N_2PCl$. Calculated %: P 8.54; N 7.70.

f) A diazo solution prepared from 2.07 g of amine was coupled in a medium of sodium acetate with 4.40 g of chromotropic acid. The azo dye was isolated by acidification with hydrochloric acid, reprecipitated from water by hydrochloric acid, and washed with hydrochloric acid. Yield 2.6 g of dark-crimson solid. λ_{max} 520 mμ.

Found %: P 5.59, 5.59; S 11.47, 11.87; Cl 6.34, 6.00; Na 3.61. $C_{16}H_{11}O_{11}S_2PClNa$. Calculated %: P 5.52; S 11.44; Cl 6.32; Na 4.10.

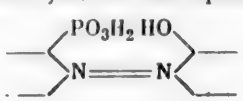
SUMMARY

1. The only method described in the literature for preparation of o-aminobenzenephosphonic acid from o-bromobenzenephosphonic acid did not give satisfactory results when checked.

2. An investigation of the reaction of PCl_3 with o-nitroaniline diazonium fluoborate established the formation not of the expected o-nitrobenzenephosphonic acid, but of chloro-o-aminobenzenephosphonic acid. Its formation is the consequence of three reactions which appear to proceed in parallel: a) replacement of the phosphonic group by the diazo group; 2) reduction of the nitro group; 3) chlorination.

3. Chloro-o-aminobenzenephosphonic acid could be isolated via its copper complex.

4. Starting from the prepared acid, six azo dyes, the first representatives of a class containing the grouping



were synthesized.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

THE LACTONES OF D-IDOSACCHARIC ACID

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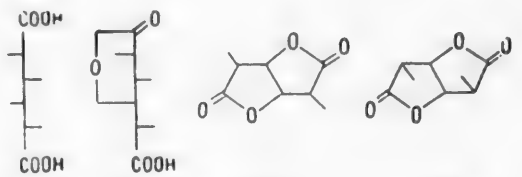
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4076-4079, December, 1960
Original article submitted January 26, 1960

The D- and L-idosaccharic acids are the least investigated of the ten stereoisomeric tetrahydroxyadipic acids. Both enantiostereoisomers in the form of uncrystallizable syrups were first isolated by Fischer and Fay in 1895 [1]; D-idosaccharic in the crystalline form was only obtained in 1945 by Seebeck, Sorkin, and Reichstein [2], who also describe the preparation, using a phenylhydrazine salt, of the monophenylhydrazide of D-idosaccharic acid from the lactone which had not been separated in a pure form. With the exception of this reference there has been no published information up to the present time regarding the lactones of idosaccharic acids.

Owing to the "antisymmetry" of the configuration of the carbon chain [3] the idosaccharic acids, and also the mannosaccharic acids, can theoretically form only a single γ-monolactone (II). It is known that allomucic and mucic acid can each form two enantiostereoisomeric γ-monolactones, and glucosaccharic and talomucic acids, two diastereoisomeric γ-monolactones each [4, 5]. The monolactones of the mannosaccharic acids have not yet been isolated, but it is known that mannosaccharo-γ,γ-dilactones (III) are very easily formed. The unusually large difference between the specific rotation of D-idosaccharic acid (+15.6°) [2] and the specific rotation observed by Fischer for the syrupy forms of the idosaccharic acids (more than −100 and +100° for the D- and L-enantiostereoisomers respectively [1], suggests that idosaccharic acids also may be able to form γ,γ-dilactones (IV).

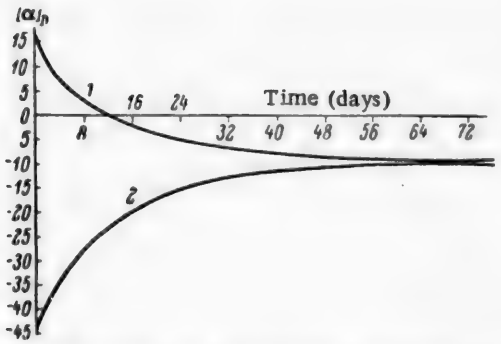


We fractionated the syrup obtained by decomposing calcium D-idosaccharate with oxalic acid [2] and evaporating the filtrate under vacuum with acetone according to the method described by Steiger and Reichstein for the lactones of D-talomucic acid [4], and thus we succeeded in separating a crystalline substance whose aqueous solution was strongly levorotary ($[\alpha]^{18}D$-43.6°). This substance behaved as a monolactone when it was titrated with a solution of alkali, i.e., only one COOH-group was titrated in the cold, and two COOH-groups after heating; the neutralization equivalent together with the elementary analysis indicates that we are dealing with a previously unknown monolactone of D-idosaccharic acid. Although the specific rotation, and especially the shifting of the rotation toward the left in the conversion of acid to lactone, indicates the presence of the γ-lactone ring (II) and excludes in principle the possibility of the δ-lactone structure (V), nevertheless we studied the mutarotation of the lactone and were convinced that the character of the latter actually corresponds to the mutarotation of γ-lactones (see figure). The results of these measurements in conjunction with data on the mutarotation of D-idosaccharic acid [2] enabled us to determine the kinetics of the formation and hydrolysis of the lactone, using equations cited previously [5]. The essential kinetic data are presented in the table.

Essential Kinetic Data on the Formation and Hydrolysis of D-Idosaccharomonolactone

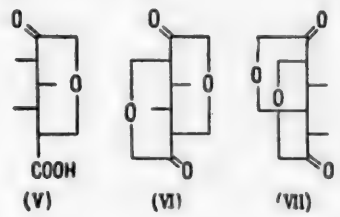
Starting material	α_0	α	$K_1 + K_2$	K_1	K_2	$\frac{K_1}{K_2}$
D-Idosaccharic acid (I) [2]	+15.6°	−9.3°	0.0033	—	—	—
D-Idosaccharomonolactone (II)	−43.6°	−9.8°	0.0030	0.00184	0.00136	1.353

Note: α_0) Initial specific rotation; α) specific rotation of the equilibrium mixture; K_1) velocity constant of hydrolysis of the lactone; K_2) velocity constant of conversion of acid to lactone (K_1 and K_2 are expressed in hour^{-1}). Temperature 18 ± 2°.



Curves showing the formation and hydrolysis of D-idosaccharomonolactone. 1) D-Idosaccharic acid [2]; 2) monolactone.

As shown by the table, the constants for the formation and hydrolysis of D-idosaccharolactone are very close to the corresponding constants for the monolactones of D-talomucic acid [5].



(V) (VI) (VII)

After 12 hr heating of the monolactone under vacuum at 100° we obtained an uncrystallizable, extremely viscous, light-yellow syrup, an aqueous solution of which was strongly levorotary ($[\alpha]^{19}D$ −106.8°). The volume of alkali solution required to neutralize the substance after heating corresponded to the presence of two COOH-groups; the neutralization equivalent and the elementary analysis showed that the syrupy material is a dilactone; its structure must correspond to Formula (IV) because the formation of a δ,δ-(VI) or a δ,γ-dilactone (VII) is very improbable in the case of idosaccharic acids. The substance gave a strongly acidic reaction in water (pH below 3); it is interesting to note that solutions of D-glucosaccharodilactones are also acidic (to Congo Red) [6]; E. Fischer observed a strongly acidic reaction in the case of the aqueous solution of his syrupy D-idosaccharic acid, and a specific rotation of less than −100° [1]. The compound which we prepared differs from the dilactones of mannosaccharic, glucosaccharic [6], and 2-desoxyglucosaccharic acids [7] in that it did not reduce Fehling's solution. A more detailed investigation of this compound was not possible because the quantity was very small.*

EXPERIMENTAL

D-Idosaccharomonolactone (II). D-Idosaccharic acid (I) was prepared from D-xylose through D-idonic acid according to the method described by Fischer and Fay [1], and modified by Reichstein and co-workers [2]. 2,4,3,5-Di-O-benzylidene-D-idonic acid was separated directly from a mother liquor containing D-gulonolactone [8]. The syrup obtained by decomposing calcium D-idosaccharate with oxalic acid and evaporating the filtrate under vacuum was fractionated with acetone by Steiger and Reichstein's method for preparing the monolactones of talomucic acid [4]. Acetone was added to the syrup, the precipitated D-idosaccharic acid was filtered off and the filtrate was evaporated in a vacuum to the consistency of a thick syrup, which was triturated with acetone and the D-idosaccharic acid which crystallized out was filtered off (after recrystallization from acetone its m.p. was 148-150°). The acetone mother liquor was evaporated under vacuum to the consistency of a syrup,

*D-Idosaccharic acid is one of the least available of the tetrahydroxyadipic acids. The yield of the crystalline D-idosaccharomonolactone was less than 2% of the original quantity of D-xylose.

dried immediately at 85° and again diluted with acetone; the evaporation and drying were repeated. The resulting colorless viscous syrup crystallized after standing in the cold for two weeks. It was reprecipitated from a concentrated aqueous solution (syrup) with acetone, washed with cold acetone and dried; m.p. 166-168° (dec.), $[\alpha]^{18}D$ −43.6 (c 1.078, water, 15 min after dissolving). The titration of 18.8 mg of the material to the phenolphthalein end-point at 0° required 5.00 ml of 0.02 N NaOH, and at 100° 9.90 ml 0.02 N NaOH; equivalent weight 188; calculated for $C_6H_8O_7$ 192.

Found %: C 37.20; H 4.30. $C_6H_8O_7$. Calculated %: C 37.49; H 4.20.

D-Idosaccharodilactone (IV). The monolactone (II) was heated under vacuum in a thick-walled test tube at 100° for 12 hr. A light-yellow, extremely viscous syrup formed which did not crystallize; $[\alpha]^{19}D$-106.8° (c 1.020, water, 15 min after dissolving). The solution was acid to Congo Red and did not reduce Fehling's solution. The titration of 20.6 mg of the material to the phenolphthalein end-point required 12.10 ml of 0.02 N NaOH (by titrating the excess alkali after heating and boiling); neutralization equivalent 85.1.

Found %: C 40.98; H 3.56. M 170.2. $C_6H_6O_6$. Calculated %: C 41.37; H 3.47. M 174.

The polarimetric measurements and the calculation of velocity constants were made according to methods and equations described previously [5].

SUMMARY

1. The previously unknown γ-monolactone and dilactone of D-idosaccharic acid were prepared.
2. The velocity constant of hydrolysis of D-idosaccharomonolactone was measured polarimetrically.

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THE INTRAMOLECULAR HYDROGEN BOND AND DIPOLE MOMENTS OF ORGANIC COMPOUNDS

VII. PHENYLAZO, CARBOXYL AND CARBOMETHOXY SUBSTITUTED NAPHTHOLS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4080-4085, December, 1960
Original article submitted October 24, 1959

The study of the dipole moments (μ) of compounds with intramolecular hydrogen bonds (IHB) [1]* was continued with phenylazo-, carboxyl- and carbomethoxynaphthols. The values of μ for 2- and 4-hydroxy-1-phenylazonaphthalenes and their methyl esters were determined in benzene and dioxane, while those of 2- and 4-carboxy-1-hydroxynaphthalenes, 3-carboxy-2-hydroxynaphthalene and some of their methyl esters were usually determined only in dioxane because of the difficulty of dissolving them in benzene. Measurements of the dielectric permeability factor $\varepsilon_{1\,2}$ and of the density $\rho_{1\,2}$ of these solutions at various concentrations of the dissolved substance (in moles) N_2 have been published [2], while calculated values of the molar polarization of the dissolved substance at infinite dilution $P_{2\infty}$, of the electron and atomic polarization P_{E+A} and of μ in Debyes (D) are shown in Table 1. In the calculation P_A was taken as equal to 0.05 P_E. The value of μ obtained for 2-hydroxy-1-phenylazonaphthalene in benzene corresponds closely with the value in the literature (1.60 D) [3]; the values of μ in the literature for 4-hydroxy-1-phenylazonaphthalene in dioxane and for its methyl ester dissolved in benzene are from 1.5-2 times lower than those obtained by us.

The previously proposed criteria for IHB based on values of μ [1] indicate the presence of a bond of this type in 1,2-phenylazonaphthols. As a matter of fact, 1-phenylazo-2-hydroxynaphthalene, analogous to other compounds with a bond of this type (Table 2), has an appreciably lower moment than 1-phenylazo-4-hydroxynaphthalene; in contrast to the latter, an increase in the moment is observed in the case of the methyl ester of 1-phenylazo-2-hydroxynaphthalene; its moment in dioxane, in comparison with benzene, changes in the same direction as in the case of the esters. These same correlations of the moments are also observed in the case of the phenylazophenols, inasmuch as μ of the ortho isomer of these compounds is less than that of the para isomer by 0.31 D; in the para isomer, as in 1-phenylazo-4-hydroxynaphthalene, the transition to the methyl ester is accompanied by a decrease in the moment, as also in the case of the naphthols, while in using dioxane as a solvent μ increases on a considerably greater scale than in the case of the esters. Thus the dipole moments confirm the presence of an IHB in 1,2-azonaphthols; it is also confirmed by the data for their absorption in the infrared [7-9] and the ultraviolet [10] bands of the spectra and also, apparently, from some of their chemical [11] and macrophysical [12] properties.

From Table 2 it is evident that both carboxyl- and carbomethoxy substituents of naphthols, which can form an IHB with the naphthol hydroxyl, display qualitatively characteristic correlations of the dipole moments of isomers (for compounds with this type of bond), in comparison with esters, when benzene is replaced by dioxane as the solvent, etc. The closeness of the observed moment (2.83 D in dioxane) to that calculated for a structure with a fixed cis-position of the corresponding functional groups (2.53 D) (I), confirms the presence, for example, of an IHB in 2-carboxy-1-hydroxynaphthalene. Particular consideration should be given to 2-carboxy-2-methoxynaphthalene, for which, by analogy with o-methoxybenzoic acid, one can assume the presence of an IHB of type (II) [5] or an equilibrium between (II) and (III), in benzene solution [13].

*[1] combines papers I-VI.

TABLE 1

Values of μ (in D) and $\Delta\mu$ of Disubstituted Derivatives of Naphthalene

$C_{10}H_6XY$		$P_{2\infty}$		P_{E+A}	μ (D)		μ (D) values from literature	$^{\mu}C_{10}H_6XY$ (D) [5, 7]		$\Delta\mu = {}^{\mu}C_{10}H_6XY - {}^{\mu}C_{10}H_8XY$		μ (D), calc. according to [6]
X	Y	in benzene	in dioxane		in benzene	in dioxane		in benzene	in dioxane	in benzene	in dioxane	
1-$N_2C_6H_5$	2-OH	134.1	148.9	76.5	1.67	1.90	1.60 (b) *	1.31	—	+0.36	—	—
1-$N_2C_6H_5$	2-OCH_3	153.3	172.5	81.3	1.87	2.10	—	—	—	—	—	—
1-$N_2C_6H_5$	4-OH	—	283.7	76.5	—	3.17	2.1 (d) **	1.62	2.04	—	+1.13	1.89
1-$N_2C_6H_5$	4-OCH_3	144.5	160.7	81.3	1.75	1.96	0.93 (b) *	1.29	+	+0.46	—	1.39
2-COOH	1-OH	—	194.3	53.1	—	2.83	—	—	2.63	—	+0.20	—
2-COOH	3-OH	—	283.7	53.1	—	3.34	—	—	2.63	—	+0.71	—
2-COOH	3-OCH_3	793.4	324.6	58.0	5.97	3.59	—	5.52	—	+0.45	—	—
1-COOH	4-OH	—	316.7	53.1	—	3.57	—	—	2.73	—	+0.84	2.68
1-COOH	4-OCH_3	—	267.7	58.0	—	3.19	—	—	—	—	—	2.34
2-$COOCH_3$	3-OH	244.0	269.2	58.0	3.00	3.20	—	2.47	—	+0.53	—	—
2-$COOCH_3$	3-OCH_3	202.3	—	62.8	2.60	—	—	2.68	—	−0.08	—	—
1-$COOCH_3$	4-OH	—	337.4	58.0	—	3.69	—	—	2.8 (C_2H_5)	—	~ +0.8	—

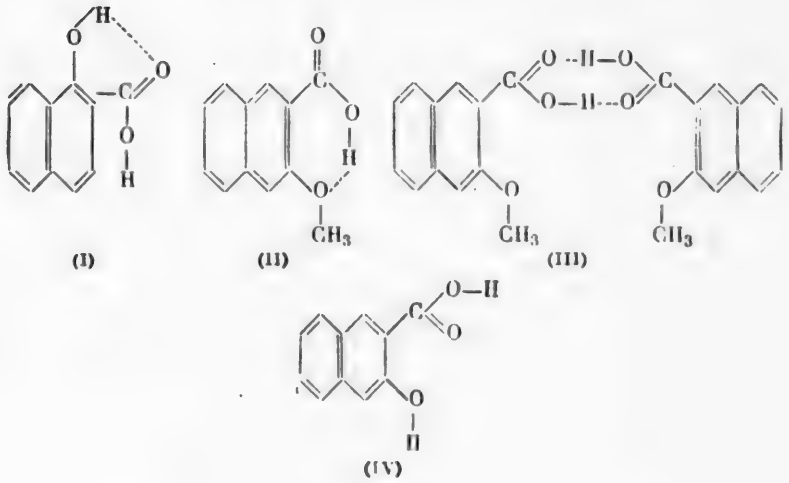
*Solvent — benzene.

**Solvent — dioxane.

TABLE 2

Relationship of Values of μ (in D) of Disubstituted Derivatives with an IHB

$C_{10}H_6XY$		$\mu_{1,4} - \mu_{1,2}$ (benzene)	$\mu_{OCH_3} - \mu_{OH}$ (benzene)	μ dioxane $-$ μ benzene
X	Y			
1-$N_2C_6H_5$	2-OH	+1.27 (d) *	+0.20	+0.23
2-COOH	1-OH	+0.74	—	—
2-COOH	3-OH	—	+0.25	—
2-$COOCH_3$	3-OH	—	—	+0.20
1-CHO	2-OH	—	+0.30	+0.03
1-$COOCH_3$	2-OH	+1.43 (d)	+0.18	−0.02
1-NO_2	2-OH	+1.38	+0.15	+0.22
1-$N_2C_6H_5$	4-OH	—	−1.21 (d)	—
4-COOH	1-OH	—	−0.38 (d)	—
1-$COOCH_3$	4-OH	—	−0.44 (d)	—
1-NO_2	4-OH	—	−0.08	+0.61
1-$N_2C_6H_5$	2-OCH_3	−0.12	—	+0.23
1-$N_2C_6H_5$	4-OCH_3	—	—	+0.21
1-NO_2	2-OCH_3	+0.15	—	+0.13



(I) (II) (III) (IV)

*Solvent — dioxane.

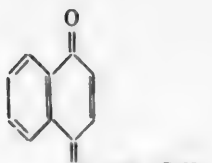
As a matter of fact, 2-carboxy-3-methoxynaphthalene in benzene in contrast to 2-carbomethoxy-3-hydroxy- and 2-carbomethoxy-3-methoxynaphthalenes has an unusually high moment (5.97 D) for that type of compound, while o-methoxybenzoic acid has μ = 5.52 D; in dioxane the moment falls sharply and takes the usual value for hydroxy- and methoxynaphthoic acids. The value calculated for structure (II) was found to be 4.55 D, and if one takes into consideration the superposition of a high moment of interaction of groups in the case of orthodisubstituents, especially of naphthalene, then structure (II) with an IHB formed by the participation of a carboxy hydroxyl, appears highly probable. In benzene, with increasing concentration of acid, the value $\frac{\Delta\varepsilon_{1,2}}{\Delta N_2}$ gradually falls from 51.6 when N_2 = 0.000186 to 46.5 when N_2 = 0.001991 (according to the literature [5] the same thing occurs with o-methoxybenzoic acid), which is not observed in dioxane nor with 2-carbomethoxy-3-hydroxynaphthalene in benzene. Evidently, with increasing concentration in benzene, structure (II) breaks down, and equilibrium is displaced in the direction of structure (III). In dioxane, structure (II) is absent altogether.

Phenylazo-, carboxyl- and carbomethoxy substituted hydroxy- and methoxynaphthalenes (except 2-carbomethoxy-3-methoxynaphthalene) have a noticeably higher moment in comparison with the corresponding

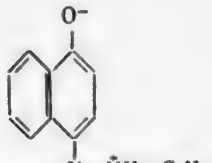
substituents of benzene, which confirms the previously made inference [1] concerning the positive value of $\Delta\mu$ = $= \mu_{C_{10}H_6XY} - \mu_{C_6H_4XY}$ in the case of practically all disubstituents in the same naphthalene ring. This apparently occurs with moments measured in benzene as well as in dioxane, and also in compounds in which the corresponding monosubstituents of naphthalene possess moments either larger or smaller than those of the same substituents of benzene. Data for phenylazonaphthols and their methyl esters (as well as for 1,4-dimethoxynaphthalene [14] and naphthalic acid anhydride [15]) show that $\Delta\mu$ is positive for disubstituents containing functional groups with the same or opposite effect on the displacement of electrons in the coupling of their n- or π-electrons with π-electrons of the ring system. The positive character of $\Delta\mu$ may be explained, first of all, by an increase in the degree of double-bondedness of the C_1-C_2 and C_3-C_4-bonds in the naphthalene nucleus, and hence in the degree of conjugation of the functional groups. This also explains the increase in acidity [16], and the larger displacement (than in the case of disubstituted benzene) $\nu_{C=O}$ (frequency of the valence oscillation C = = O) in the infrared spectrum [17] and of the long wave absorption bands in the ultraviolet [18]. However in disubstituents with functional groups having the same electron displacing effect, the increase of μ owing to coupling is apparently absent, and the positive character of $\Delta\mu$ must be explained by other reasons, principally by the increase of the induced moment in groups, and by the steric effect of para-hydrogen which hinders the free rotation of groups in positions 1 and 4 [14] and, possibly, contributes to the greater strength of compounds with an IHB [19].

From the point of view of explaining the fine structure of naphthalene, the values of μ for various disubstituted compounds with the same functional groups at different neighboring hydrogen atoms of the same ring are of interest. Thus, the dipole moment in dioxane of 2-carboxy-3-hydroxynaphthalene exceeds that of 2-carboxy-1-hydroxynaphthalene by 0.51 D. Both these compounds undoubtedly contain an IHB, which is indicated by the criteria previously described (Table 2), and also by the greater proximity of the first value of μ to that calculated for structure (I) than to that calculated for structure (IV) without an IHB (calculated moment 1.43 D). This increase of μ cannot be caused in the first case by the presence of some fraction of molecules with IHB of type (II), inasmuch as its moment differs only slightly from that of 2-carbomethoxy-3-hydroxynaphthalene. In view of the lower degree of double-bondedness of the C_2-C_3-bond in naphthalene, it cannot be explained by the superposition of further increased values of the moment in 2,3-disubstituents, caused by the coupling of functional groups. It is apparently caused primarily by the greater strength of the IHB in the 1,2- than in the 2,3-disubstituent. It is precisely this fact that explains the greater displacement $\nu_{C=O}$, observed in the former in comparison with the latter in the case of many disubstituted naphthalenes with carbonyl-containing functional groups [17, 19]. Other possible reasons for the increase of the moment in 2,3-disubstituted (compounds) may be the degree of deviation from coplanarity of the functional groups with the ring, and also the effect of induced moments.

Dipole moments make it possible to determine the structure of molecules in the basic state more unambiguously than electron spectra or chemical properties. Thus, the proximity of the values of μ (in benzene) of o-phenylazophenols and of phenol, of the methyl ester of p-phenylazophenol and of anisole gives evidence of the presence in the former of an azostructure, which is in accordance with data on their infrared spectra [8]. The proximity of the value of the moment of 1-phenylazo-2-hydroxynaphthalene to that of 2-naphthol gives evidence of the same kind of structure, but this, however, does not correspond with deductions made from absorption spectra in the infrared and in the ultraviolet [8, 10, 20, 21]. In the case of 1-phenylazo-2-methoxy- and 1-phenylazo-4-methoxynaphthalenes and especially in the case of 1-phenylazo-4-hydroxynaphthalene in contrast to the compounds mentioned, a considerably larger moment is observed than in the case of the corresponding hydroxy- and methoxynaphthalenes (by 0.5-1.28 D). A similar increase in the moment is also observed in some substituted azobenzenes, for example, in p-amino, p-nitro- and p-N,N-dimethylaminobenzene (by 0.90, 0.50 and 1.64 D, respectively [21]). On the basis of inferences from the data on absorption in the infrared and ultraviolet regions of the spectrum [8, 10, 21] one can assume that the increased moment noted in the case of 1-phenylazo-4-hydroxynaphthalene is brought about principally by the transformation of part of the molecules into a quinone–hydrazone structure (V) with some subsequent displacement of charges (VI). The calculated moment for structure (V) is approximately equal to 4.8 D ($\mu_{C=O}$ 2.9 D; μ of the group = $NNHC_6H_5$ is taken as equal to the moment of benzaldehydephenylhydrazone 1.93 D), while for structure (VI) it is more than 30 D. In order to explain this increase in the moment it would be necessary to assume the presence of approximately 30% of the molecules with structure (V) or a sum total of 1% of the molecules with structure (VI).



(V)



(VI)

However the assumption concerning the transition from the azo- to the hydrazoquinone structure is unsatisfactory for explaining the increase of the moment in the methyl ester of phenylazonaphthols and in N,N-dimethylaminoazobenzene. In this case the increase in the moment may be principally explained by the observed increase in the effect of coupling of the substituent with the benzene ring in the presence of an azo group which lengthens the conjugated chain [22]. However it remains unclear why this fails to occur in some substituted azobenzenes, such as p-halogen- or p-hydroxy-, in which the value of μ is practically identical with that of the corresponding substituents of benzene. The question also remains open as to what extent the trans form of the phenylazo group is preserved in these compounds since a slight deviation from this can bring about a noticeable increase in the moment (the μ of the trans-azobenzene is equal to zero, while the cis- is 3.0 D [3, 23]).

SUMMARY

1 The dipole moments of 1,2- and 2,1-phenylazonaphthols and their methyl esters, and also 1,2-, 2,3- and 1,4-hydroxynaphthoic acids and their methyl ethers and methyl esters, were determined at 25° in benzene or dioxane as solvents

2. 1,2- and 2,3-Azo- and carboxy- or carbomethoxy- substituted naphthols, according to data on their dipole moments, contain a strong intramolecular hydrogen bond. 2-Carboxy-3-methoxynaphthalene has a weak bond of this kind with the hydrogen of the hydroxyl of the carboxyl group.

3. The value of $\Delta\mu = \mu_{C_{10}H_6XY} - \mu_{C_6H_4XY}$ for substituents in the same naphthalene ring, with a few exceptions, is positive, which is brought about by the increase in the degree of double-bondedness of the C_1-C_2 and C_3-C_4-bonds in naphthalene, by the increase of the induced moment in functional groups, and by the steric effect of para-hydrogen atoms.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

THE INTRAMOLECULAR HYDROGEN BOND AND DIPOLE MOMENTS OF ORGANIC COMPOUNDS

VIII. 2,4- AND 4,6-DIACETYLRESORCINOLS AND THEIR METHYL ESTERS

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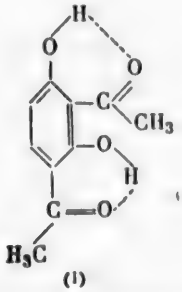
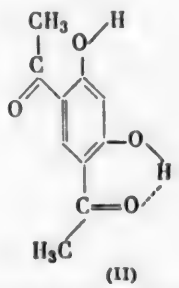
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4085-4088, December, 1960
Original paper submitted October 24, 1959

Differences in the macrophysical properties (melting and boiling points, volatility with steam, solubility in benzene, etc.) and in the ultraviolet absorption curves [2] of 2,4- and 4,6-diacetylresorcinol serve as a foundation for the assumption of the presence in the former of two (I), and in the second of only one (II), intramolecular hydrogen bond (IHB).



(I)



(II)

This difference in molecular structure is regarded as experimental proof of the complete or partial fixation of one of the Kekule structures (in the formation of an IHB) and of the obligatory presence, for a strong IHB, of a double bond between corresponding carbon atoms of the benzene ring [1, 3]. However structures (I) and (II) cannot be coordinated with a number of other properties of the molecules of the observed compounds. In the Raman spectra of both 4,6- and 2,4-diacetylresorcinols there is only one frequency of valence vibration of the carbonyl group [4]; in both cases absorption in the region of the OH-group is absent in the infrared [5]. Moreover, the difference in the macrophysical properties of these substances may be the result of other peculiarities of the observed molecules—with their form [4, 6], for example—while the difference in the electron spectra may be due to a difference in the excited state and not merely in the fundamental state of the molecules. In this connection it is therefore advisable to examine other properties of 2,4- and 4,6-diacetylresorcinols which are characteristic of the fundamental state of the molecules, and especially their dipole moments.

The values of the dipole moments (μ in D) of 2,4- and 4,6-diacetylresorcinols and their dimethyl esters were determined at 25° in benzene and in dioxane solutions as described previously [7]. The compounds to be studied were synthesized in accordance with information in the literature [8].* The values for molar polarization

*Some of the compounds investigated were synthesized by B. G. Distanov and kindly offered to us for measurement.

($\varepsilon_{1,2}$) and ($\rho_{1,2}$) in debyes shown in the table were calculated on the basis of measured values of the dielectric permeability $P_{2\infty}$ and μ and the density of the solutions. In calculating the values of the electronic and atomic polarizations P_{E+A} it was assumed, considering the high polarity of the materials being examined, that $P_A = 0.15\ R_D$, where R_D is the molar refraction of the dissolved substance (which was calculated as the sum of the values of the refractions of the separate bonds). The value of μ in the table is the average of at least two series of measurements of $\varepsilon_{1,2}$ and $\rho_{1,2}$ of solutions of various concentrations.

The observed values of the moment confirm that 2,4-diacetylresorcinol has structure (I) with two hydrogen bonds within the molecule. This follows from the fact that the moment of this compound is near or even coincides with that of 2-hydroxyacetophenone (2.78 D [10] in benzene and 2.86 D [11] in carbon tetrachloride) and with the value of the moment (3.15 D), calculated from the moments of the separate bonds [12] for the configuration in which both hydroxyl and carbonyl groups are located in pairs in a cis-position to each other—a position fixed by the formation of strong intramolecular hydrogen bonds. Structure (I) is further confirmed by the fact that the dimethyl ester of 2,4-diacetylresorcinol, as well as the esters of other compounds with a strong intramolecular hydrogen bond [7, 10, 13], possesses a somewhat larger moment than the initial hydroxy compound, and that $\Delta\mu = \mu_{dioxane} - \mu_{benzene}$ of the latter is lower than that of its ester.

Dipole Moments of Diacetylresorcinols and Their Methyl Esters

Compound	$P_{2\infty}$ in benzene	$P_{2\infty}$ in dioxane	P_{E+A}	$\mu \cdot 10^{18}$ in benzene	$\mu \cdot 10^{18}$ in dioxane	$\Delta\mu = \mu_{dioxane} - \mu_{benzene}$
2,4-Diacetylresorcinol. . . .	262.8	318.0	59.1	3.14	3.54	+0.40
Dimethyl ether of 2,4-diacetylresorcinol. . . .	296.8	376.6	70.0	3.33	3.85	+0.52
4,6-Diacetylresorcinol. . . .	490.1	262.2	59.1	4.56	4.93	+0.37
Dimethyl ether of 4,6-diacetylresorcinol.	1217.4	1417.1	70.0	7.45	8.07	+0.62

*Some of the investigated substances were synthesized by B. G. Distanov; he was kind enough to submit them for measurement.

The dipole moment of 4,6-diacetylresorcinol, in contrast to that of 2,4-diacetylresorcinol, appreciably exceeds that of 2-hydroxyacetophenone (by a factor of 1.64) and, almost to the same extent as the moment of its dimethyl ester, it exceeds that of 2-methoxyacetophenone (by a factor of 1.87). In other respects 4,6-diacetylresorcinol acts similarly to 2,4-diacetylresorcinol or 2-hydroxyacetophenone, i.e., to compounds without free hydroxyls. On conversions to the ester it shows a significant increase in moment (by a factor of 1.63)—even greater than 2-hydroxyacetophenone does when it is converted to 2-methoxyacetophenone (by a factor of (1.43). Its moment, measured in dioxane, increases in comparison with that measured in benzene, but it is only half as large as that of the ester, and even less than that of 2,4-diacetylresorcinol, which indicates the strength of the hydroxyl bond in the molecule. Apparently, in 4,6-diacetylresorcinol both hydrogens of the hydroxyls take part in the formation of fairly strong intramolecular hydrogen bonds. Comparison of the observed moment of 4,6-diacetylresorcinol with that calculated (5.45 D) from the moments of the separate bonds [12] for the structure with two hydrogen bonds which fix the cis-position of the corresponding functional groups in the plane of the ring does not contradict this. A somewhat lower value of the observed moment in comparison with the calculated value (by 0.89 D in benzene) indicates the same phenomenon in the case of 2-hydroxyacetophenone, whose moment in benzene is lower than that calculated from the moments of the bonds [12] (3.15 D) by 0.37 D. This discrepancy is connected either with the inaccuracy of the calculation of μ for the cis-configuration (according to other data the value of μ, calculated for the cis-structure of 2-hydroxyacetophenone is 2.8 D [14]), or with the superposition of other interactions of the functional groups that are hard to account for. Among these is the observed deviation of their position from coplanarity with the ring.

It is evident that data on the dipole moments of these compounds may be satisfactorily coordinated with the assumption that there are two intramolecular hydrogen bonds present both in 2,4- and in 4,6-diacetylresorcinol and, consequently, that in the formation of this type of bond there is a lack of fixation of one of the Kekule

structures [3]. Recently [15] this was confirmed on the basis of infrared spectra of a series of disubstituted 5,6,7,8-tetrahydronaphthalenes containing an intramolecular hydrogen bond. This is also indicated by the values for the bond lengths between carbon atoms in the rings of such compounds as salicylic acid [16].

SUMMARY

1. The values of the dipole moments of 2,4- and 4,6-diacetylresorcinols and their methyl esters were determined at 25° both in benzene and in dioxane.

2. The values of the moments of the substances studied agree with the assumption that two intramolecular hydrogen bonds are present both in 2,4- and in 4,6-diacetylresorcinol.

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STUDIES IN THE NAPHTHALENE SERIES

XX. THE REACTION KINETICS OF α-NAPHTHOL WITH AQUEOUS SOLUTIONS OF AMMONIA AND AMMONIUM SULFITE*

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4089-4092, December, 1960
Original article submitted January 22, 1960

Having studied the kinetics of amination of β-naphthol [1] and having confirmed the reaction mechanism, which was explained for the first time by N. N. Vorozhtsov [2], we investigated this reaction with α-naphthol also. Only one paper [3] has been devoted to the kinetics of amination of α-naphthol derivatives

Investigation of the reaction kinetics of α-naphthol (m.p. 94°) with aqueous ammonia in the presence of ammonium sulfite was carried out in a rotating steel autoclave similar to that described by us in the study of β-naphthol [1]. Thirty minutes after complete cooling with cold water, the autoclave was opened for unloading. The entire contents of the autoclave were rinsed into a glass container with water. The precipitate was filtered off and washed with a 5% solution of sodium hydroxide until the presence of naphthol could no longer be detected.

TABLE 1

Dependence of Reaction Velocity on Concentration of Ammonia

Concentration NH_3 (%)	20.0		14.7		10.3		8.16	
C_a	11.79		8.63		6.04		4.8	
C_c	0.38		0.38		0.38		0.38	
a (%)	57.5	57.3	42.4	49.1	27.3	31.1	28.6	49.8
Temperature	170.0°	170.1°	170.0°	170.4°	169.9°	169.7°	169.8°	169.9°
$K_1 \cdot 10^{-2}$	2.42	2.44	3.77	3.12	5.70	5.14	5.50	6.12
$K_1 \cdot 10^{-2}$ avg.	2.35		3.64		5.42		5.81	
$K_2 \cdot 10$	2.86	2.88	3.25	2.69	3.44	3.10	2.64	2.93
$K_2 \cdot 10$ avg.	2.79		3.14		3.27		2.78	

Note: Experimental conditions: 5.50 g α-naphthol, 5.1 g $(NH_4)_2SO_3$, 100 ml 8-20% ammonia, 170°, 60 min. The values are averages of four experiments.

*For Report XIX, see Zh. O. Kh. 30, 2714 (1960).

TABLE 2

Dependence of the Reaction Velocity Constant on the Concentration of α-Naphthol

Quantity of naphthol (g)	2.736		5.472		8.208	
a (%)	63.8	60.8	57.5	57.3	58.3	58.3
Temperature	169.9°	169.9°	170.0°	170.1°	170.0°	170.0°
$K_2 \cdot 10$	2.55	2.3	2.86	2.88	2.79	2.79

Note: Reaction conditions: 100 ml of 20.4% ammonia, 5.1 g $(NH_4)_2SO_3$, 170°, 60 min.

TABLE 3

Dependence of the Reaction Velocity Constant on the Quantity of Ammonium Sulfite

Quantity of $(NH_4)_2SO_3$ (g)	2.21		4.41		6.61	
C_c	0.19		0.38		0.57	
C_a	11.8		11.79		11.8	
a (%)	79.0	79.0	57.5	57.3	36.8	38.6
Temperature	169.7°	169.9°	170.0°	170.1°	169.9°	170.0°
$K_2 \cdot 10$	2.43	2.43	2.86	2.88	3.44	3.28

Note: Reaction conditions: 5.50 g α-naphthol, 100 ml 20.4% ammonia, 170°, 60 min.

TABLE 4

Dependence of the Reaction Velocity Constant on the Length of the Experiment

Length of the expt. (in min)	60		90		120	
C_c	0.38		0.38		0.38	
a (%)	57.5	57.3	46.2	49.2	33.7	29.5
Temperature	170.0°	170.1°	170.2°	170.0°	169.8°	170.1°
$K_2 \cdot 10$	2.86	2.88	2.67	2.45	2.81	3.15

Note: Reaction conditions: 5.50 g α-naphthol, 100 ml 20.4% ammonia, 170°.

Determination of the unreacted α-naphthol was carried out as follows: to 50 ml of the combined filtrate and wash water, neutralized by hydrochloric acid using thiazole paper, 20 ml of a 2 N solution of barium chloride at 70-80°. After no more than an hour the barium sulfite precipitate is filtered off and repeatedly washed with a 0.5% solution of barium chloride. The filtrate and wash water are made slightly acid to litmus with acetic acid, 70 ml of a saturated solution of sodium bicarbonate is added and it is then titrated back with a 0.05 N solution of p-nitrophenyldiazone.

TABLE 5

Dependence of the Reaction Velocity Constant on Temperature

Temperature (°C)	150.1	150.1	159.9	160.1	170.0	170.2	170.1	169.9	180.0	179.8	190.2	183.8
C_c	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38	0.38
a (%)	84.5	84.6	72.3	76.0	57.5	60.4	57.3	53.5	37.9	38.0	28.7	28.9
K_2 experimental	0.087	0.087	0.166	0.142	0.286	0.261	0.283	0.277	0.493	0.478	0.639	0.642
K_2 experimental average	0.087		0.154		0.279				0.488		0.640	
K_2 calculated	0.084		0.152		0.268				0.460		0.774	

Note: Reaction conditions: 5.50 g α-naphthol, 5.1 g $(NH_4)_2SO_3$, 100 ml 20.4% ammonia, 60 min. Values show are the averages of four experiments.

The quantity of ammonia in the experiments corresponded to 13-50 moles per mole of α-naphthol which assured a practically constant concentration of ammonia and the presence of α-naphthol in solution during the course of the reaction at high temperature.

The reaction velocity constant for the reaction of α-naphthol with ammonia in the presence of ammonium sulfite was originally calculated according to the equation:

$$K_1 = \frac{2.303}{t \cdot C_c} \cdot \lg \frac{100}{a}, \qquad (1)$$

t is time of the reaction (in minutes), C_c is the concentration of ammonium sulfite (in moles/liter), a is the quantity of unreacted α-naphthol (in % of the original).

From the results of the experiments on the reaction of α-naphthol, ammonium sulfite and ammonia of varied concentration which are shown in Table 1, it is possible to determine the reaction velocity constant as being within the limits of from $2.35 \cdot 10^{-2}$ to $5.81 \cdot 10^{-2}$ moles/liter per min.

Taking into consideration the hydrolytic conversion of ammonium sulfite:

$$(NH_4)_2SO_3 + HOH \rightleftarrows NH_4HSO_3 + NH_4OH, \qquad (2)$$

we used the expression:

$$K_2 = \frac{2.303 \cdot C_a}{t \cdot C_c} \cdot \lg \frac{100}{a},$$

where C_a is the concentration of ammonia (in moles/liter) to determine the reaction velocity constant K_2.

Since the velocity constant (K_2), calculated according to this equation is practically constant, this indicates (just as we mentioned in the case of β-naphthol) that the velocity of the reaction between α-naphthol and ammonia in the presence of ammonium sulfite is directly proportional, not to the concentration of the latter, but instead to the concentration of ammonium bisulfite. From the data in Tables 2-4 showing the dependence of the velocity constant on the concentration of α-naphthol, the quantity of ammonium sulfite used, and the length of the experiment, the fact can be established that the magnitude of the reaction velocity constant (K_2), calculated from equation (3), is practically constant. Reaction velocity constants at different temperatures are given in Table 5. The dependence of the reaction velocity constant on temperature can be determined from the equation:

$$\lg K_2 = 11.12 - \frac{4737}{T} \pm 0.008. \qquad (4)$$

TABLE 6

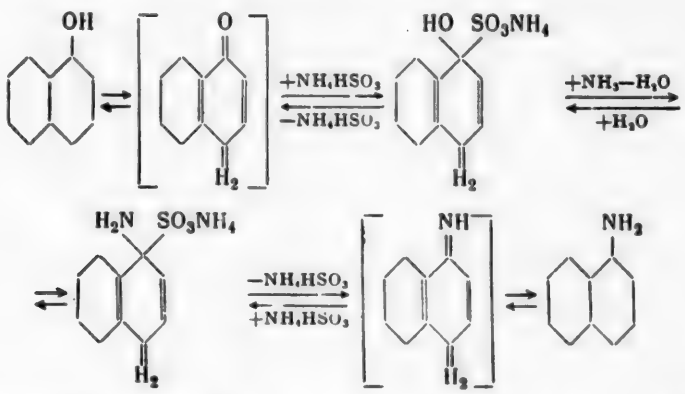
Kinetic Data on the Amination of Isomeric Naphthols

Temperature (°C)	150		160		170		180	
Naphthols	α	β	α	β	α	β	α	β
Reaction velocity constants (K_2 calculated)	0.084	0.118	0.152	0.249	0.268	0.512	0.460	1.018

Note: The activation energy (Cal/mole) of α-naphthol is 21.7; that of β-naphthol is 27.3.

The values of the constant, calculated from this equation, are shown in the last line of Table 5. They correspond fully with the constants determined experimentally. The constants determined in the experiments at 190° are somewhat smaller because of changes in the concentration of sulfite as a result of corrosion of the autoclave (actually observed). The reason for the latter, as was mentioned in the case of amination of β-naphthol, is the increase in the concentration of NH_4HSO_3 because of a continuing dissociation of $(NH_4)_2SO_3$ at high temperature with the transition of ammonia into the gas phase. From the data in Table 5, the activation energy of the reaction of α-naphthol with aqueous ammonia in the presence of ammonium sulfite may be calculated as equal to 21,700 cal/mole.

Thus, just as in the case of β-naphthol, the velocity of the whole amination process may be determined from the velocity of its first phase, namely, from the velocity of the reaction of α-naphthol with bisulfite (NH_4HSO_3 or $NaHSO_3$) in accordance with the following scheme (5):



(5)

In all probability α-naphthol reacts in the keto form precisely as shown in scheme (5) [4]. The reactions of subsequent amination of the addition product, and splitting off of a molecule of bisulfite with the formation of naphthylamine, take place at greater velocity.

Comparison of the kinetic data for the naphthol isomers given in Table 6 shows that they correspond with the known reactivities of these compounds [4-6].

SUMMARY

The kinetics of the amination of α-naphthol by aqueous ammonia in the presence of ammonium sulfite in a reaction analogous to the amination of β-naphthol were studied.

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REACTIVITY OF BONDS IN TOLUENE ON INTERACTION WITH FREE METHYL RADICALS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4092-4093, December, 1960
Original article submitted January 26, 1960

We studied the reactivity of tritium atoms occupying various positions in the toluene molecule, on interaction of the latter with free methyl radicals. The reaction was carried out through the thermal decomposition of acetyl peroxide (0.05 M) dissolved in toluenes tagged with tritium, at 60-96° [1]. The methane formed was separated from the rest of the reaction products and toluene and transferred to an internal-charge counter, where its radioactivity was determined. The specific radioactivity of the toluene used in the experiments was determined in the same counter. The radioactivities of the methane and toluene were related by the equation:

$$\left(\frac{I_m}{I_{tol}}\right)_i = \frac{K_i^T}{K_\sigma^H}, \qquad (1)$$

where: K_i^T is the rate constant of removal of a tritium atom in position i by a $CH_3\cdot$ radical; K_σ^H is the overall rate constant of removal of hydrogen atoms from the toluene molecule [2]. Since K_σ^H does not depend on the character of the tagging, the ratio of rate constants of the reactions of the methyl radical with C−T bonds in various positions may be found by means of this formula (see table).

As is evident, the interaction of $CH_3\cdot$ with C−T bonds of the methyl group proceeds very rapidly and, as calculation shows gives over 99% of all the methane formed. Hence, it may be assumed that $K_\sigma^H = 3K_{CH_3}^H$. This makes it possible, using Eq. (1), to find the ratio of pre-exponential factors and the differences among the activation energies E_i^T and $E_{CH_3}^H$ (see table).

It was found that the radioactivity of the methane increases linearly with the degree of decomposition of acetyl peroxide in titrated toluene. For this reason activity values, obtained by extrapolation to zero degree of decomposition, were used in all calculations. The slope of the straight lines (tan φ) in the coordinates, activity (I_m)−degree of peroxide decomposition (η), does not depend on temperature; tan φ_o : tan φ_m : tan φ_p = 2 : 1 : 1. This effect was explained by the interaction of the methyl radical with π-bonds of the nucleus, which results in the formation of a free radical of the cyclohexadiene type; at the end of its life the latter gives product B, in which a tritium atom is bound to a tertiary, doubly bonded carbon atom. Calculation leads to the following expression for the radioactivities:

$$\frac{I_m}{I_{tol}} = \frac{K^T}{K_\sigma} + K_m[\text{Per}]_0 \cdot \tau_i,$$

which agrees with experiment. The constant K_m is a function of the rate constants of a series of elementary acts of interaction of the $CH_3\cdot$ radical with the toluene molecule and product B. It characterizes the probability of addition of $CH_3\cdot$ to specific bonds in toluene and the mobility of tritium atoms in the addition product. Evaluation shows that the reactivity of these atoms is about 100 times as great as that of hydrogen atoms in the methyl group. Proceeding from the hypothesis that the activation energy of addition of $CH_3\cdot$ to the toluene

Tagging by tritium	K_i^T/K_n^T at 85°	$\Delta E = E_i^T - E_{CH_3}^H$ (cal/mole)	$A_i^T/A_{CH_3}^H$
Ortho-	0.76	4750 ± 100	1 ± 0.15
Meta-	0.22	7900 ± 250	23 ± 8
Para-	1	4800 ± 100	1.4 ± 0.12
CH_3 group	156	2200 ± 100	1.8

nucleus may be found by Polanyi's rule, and using Vedeneev's formula [3] to calculate the C–H bond energies, we derived the experimentally observed ratios for tan φ by calculation.

SUMMARY

1. The relative rate constants, activation-energy differences, and ratios of pre-exponential factors of the reactions of removal of tritium and hydrogen atoms from various bonds in the toluene molecule by free methyl radicals were determined.

2. It was shown that the increase in activity of the methane formed on interaction of CH_3 with toluene tagged by means of tritium in the nucleus, with the extent of the reaction, is due to the addition of CH_3 to π-bonds and the formation of products containing mobile tritium atoms.

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SYNTHESES BY MEANS OF FREE HYDROXYL RADICALS

I. OXIDATIVE DIMERIZATION OF ALIPHATIC ETHERS AND ESTERS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4094-4099,
December, 1960
Original article submitted January 28, 1960

The system $Fe^{2+} + H_2O_2$ (Fenton's reagent) is a powerful generator of free hydroxyl radicals [1-3].

$$Fe^{2+} + H_2O_2 \longrightarrow Fe^{3+} + \cdot OH + OH^-$$

In the presence of hydroxyl radicals, organic compounds undergo various conversions, depending on the class and structure of the substance [4-7]. Merz and Waters [5] studied the oxidation of lower aliphatic compounds by means of Fenton's reagent, and showed that the oxidation may go both by a chain and a nonchain mechanism. Merz and Waters also indicated the possibility in principle of the formation, besides oxidation products, of products of dimerization of organic radicals obtained as a result of attack of a carbon–hydrogen bond in the organic molecule by a hydroxyl radical and removal of the hydrogen atom:

$$R{-}H + \cdot OH \longrightarrow R\cdot + H_2O$$
$$2R\cdot \longrightarrow R{-}R$$

However, these authors did not isolate such dimeric compounds; they identified bibenzyl only in the oxidation of toluene by Fenton's reagent [6].

The products of dimerization of aliphatic acids, esters, acid chlorides, and tertiary butyl alcohol were obtained by Kharasch and co-workers [8-10] in the thermal decomposition of acetyl peroxide dissolved in these compounds.

Recently Coffman and co-workers published very interesting articles [11-13] on new syntheses, discovered by them, of difunctional compounds from monofunctional ones by means of Fenton's reagent. The authors selected reaction conditions such that the dimers were the main reaction products and were obtained in good yield. It is remarkable that these syntheses were carried out under extremely mild conditions: 10-30 min in aqueous solutions at room temperature. Coffman and co-workers oxidatively dimerized aliphatic carboxylic acids, nitriles, amines, amides, alcohols, and ketones. These authors showed that the attack of the hydroxyl radical is nonselective, as a result of which all possible isomers of the difunctional compounds are obtained. It is characteristic that the attack of the methyl radical formed on thermal decomposition of acetyl peroxide dissolved, e.g., in isobutyric acid, as Kharasch and co-workers [8] showed, is selective and is directed toward the α-position relative to the carboxyl group.

It was of interest to us to investigate the dimerization of aliphatic ethers and esters, since it is possible by this method to prepare ethers and esters, respectively, of glycols with a long chain of carbon atoms, and also esters of dibasic carboxylic acids, without going through the etherification or esterification step. Moreover, investigation of the structure of dimerization products of ethers and esters is of interest from the point of view of study of the reactivity of hydroxyl radicals.

Yield and Physical Constants of the Dimerization Products of Aliphatic Ethers and Esters

Monomer	Dimerization products	Yield (in %, reckoned on H_2O_2)	Boiling point (pressure in mm)	d_{20}^{20}	n_D^{20}	MR_D		Molecular wt.		Calc. (%)		Found (%)	
						calc.	found	calc.	found	C	H	C	H
Diisopropyl ether	$C_{12}H_{26}O_2$	3.0	55° (3)	0.8497	1.4157	60.90	59.70	202.33	211	71.23	12.95	71.75	12.95
Diethyl ether	High boiling product	0.9 r (1 mole H_2O_2)	90—155 (755)	0.970	1.3925	—	—	—	127	—	—	49.35	8.74
Ethyl acetate	$C_8H_{14}O_4$	3.4	90—160 (10)	1.0474	1.4165	42.45	41.8	174.19	170	55.16	8.03	54.61	7.74
n-Butyl acetate	$C_{12}H_{22}O_4$	7.6	95—155 (1)	0.9980	1.4468	60.92	61.5	230.27	269	62.59	9.63	63.1	9.74
	$C_{24}H_{42}O_8$	2.9	above 155 (0.5)	1.0538	1.4670	119.64	120.7	458.52	475	62.86	9.23	63.31	9.27
	Polymers	2.0	—	—	—	—	—	—	—	—	—	—	—
Isoamyl-acetate	$C_{14}H_{26}O_4$	6.6	50—134 (1)	0.9815	1.4418	70.16	69.6	258.35	243	65.08	10.15	65.34	10.59
	$C_{28}H_{50}O_8$	1.0	above 134 (1)	1.0	1.4589	—	—	514.68	415	65.33	9.79	64.42	9.77
	Polymers	2.2	—	—	—	—	—	—	—	—	—	—	—
Isoamyl formate	$C_{12}H_{22}O_4$	2.5	Up to 100 (3)	0.9103	1.4261	60.92	64.8	230.27	229	62.59	9.63	63.35	9.96
	$C_{12}H_{22}O_4$	4.6	100—138 (3)	0.9666	1.4465	60.92	63.9	230.27	230	62.59	9.63	62.98	9.23
	$C_{24}H_{42}O_8$	1.7	138—144 (2.5)	0.976	1.4622	119.64	129.2	458.52	394	62.88	9.23	63.12	9.35
	Polymers	2.6	—	—	—	—	—	—	750	—	—	—	—

Our experiments showed that even such inert compounds as ethers can give products of oxidative dimerization. Thus in the reaction of diisopropyl ether with Fenton's reagent we isolated the dimer in about 3% yield, reckoned on the hydrogen peroxide taken (at 100% yield 1 mole of hydrogen peroxide forms 0.5 mole of dimer) (see table). Under the conditions of synthesis diethyl ether is vigorously oxidized to acetaldehyde and, partially, further – to acetic acid. We could not isolate the dimer in pure form from the mixture of high-boiling products obtained in this experiment in very low yield.

On interaction of esters, particularly acetates, with Fenton's reagent two competing reactions occur: dimerization of the organic radicals formed and oxidation with the formation of carbonyl compounds.

$$RCH_2OCOCH_3 + \cdot OH \longrightarrow \underset{\searrow}{RCHOCOCH_3}{}^{*}$$
$$RCH_2OCOCH_2$$

1. a. $2RCHOCOCH_3 \longrightarrow R-CH(OCOCH_3)-CH(OCOCH_3)-R$

b. $2RCH_2OCOCH_2 \longrightarrow CH_2COOCH_2R-CH_2COOCH_2R$

2. $RCHOCOCH_3 + \cdot OH \longrightarrow RCH(OH)OCOCH_3 \longrightarrow RCH{=}O + CH_3COOH$**

Apparently, when the hydroxyl radical attacks in the α-position relative to the ether (or ester) oxygen, the subsequent process is preferentially oxidation; for attack in the β- or a more remote position, it is preferentially dimerization.

From the amounts of dimer and acetic acid isolated, one can estimate the relative amounts of dimerized and oxidized monomeric ether (or ester). Thus in the reaction of ethyl acetate with Fenton's reagent the bulk of the ester is oxidized, and only 0.034 mole of the ester per mole of hydrogen peroxide is dimerized. As the carbon chain of the alcohol radical is lengthened, the relative amount of oxidized monomer is decreased, and the yield of dimerization products is much increased. Thus, n-butyl acetate and isoamyl formate give dimerization products in about 12% yield. Not only ester dimers, but also tetramers and polymeric products are formed. In the reaction of n-butyl acetate with hydroxyl radicals 7.6% dimer, 2.9% tetramer, and 2% polymers are obtained. As a result of the parallel oxidation of monomeric esters with primary alcohol radicals, the corresponding aldehydes are formed. Thus n-butyl acetate gives n-butyraldehyde, and isoamyl acetate gives isovaleraldehyde.

We are continuing the work in the direction of further study of the synthesis conditions and the structures of the dimers obtained.

EXPERIMENTAL

Dimerization of ethers. Diisopropyl ethers. Into a 2.5-liter, fourneck, round-bottom flask provided with a stirrer, two graduated dropping funnels, and a thermometer, were put 800 ml of water, 300 ml of distilled diisopropyl ether, and 20 ml of concentrated sulfuric acid. The flask was cooled with ice water. A 485 ml quantity of ferrous sulfate solution (0.66 mole), prepared by dissolving 278 g (1 mole) of ferrous sulfate heptahydrate and 55 ml of concentrated sulfuric acid (1 mole) in 575 ml of water, and 100 ml of 22.7% hydrogen peroxide solution (0.66 mole) were added simultaneously in equivalent quantities during 10 min, with vigorous stirring. During the addition the temperature rose from 4 to 25°. The organic layer (270 ml) was separated and the water layer extracted with 300 ml of distilled diisopropyl ether. The organic layer and ethereal extracts were combined, dried with anhydrous magnesium sulfate, and the ether driven off. The high-boiling residue was distilled in vacuo. There was obtained 2.2 g of a clear, greenish liquid boiling at 55° (3 mm) and corresponding in molecular weight, molar refraction, and elementary composition to a mixture of diisopropyl ethers of hexanediols, having the general formula $C_{12}H_{26}O_2$.

*Hydroxyl radicals attack carbon–hydrogen bonds not only in the α-position relative to the ether (or ester) oxygen, but also in more remote positions, as is indicated by the wide range of boiling points and refractive indices of the dimers obtained (see table).

**Here the nonchain scheme of ester oxidation is adopted in conformity with the data of Merz and Waters [5].

Diethyl ether. Into the reaction flask were put 450 ml of diethyl ether "for anesthesia" and 800 ml of water. The flask was cooled to 0° with an ice-salt mixture. With vigorous stirring, 485 ml of ferrous sulfate solution (0.66 mole) and 100 ml of 22.7% hydrogen peroxide solution (0.66 mole) were simultaneously added in equivalent quantities. The addition took 10 min, and the temperature of the reaction mass rose to 20°. The organic layer (150 ml) was separated, and the water layer was extracted with 300 ml of diethyl ether. The combined organic layer and ethereal extracts were washed with 5% sodium bicarbonate solution and dried with anhydrous magnesium sulfate. The ether was driven off and the high-boiling residue (about 1 ml) distilled from a small Claisen flask. There was obtained 0.6 g of a yellowish liquid boiling at 90-150° (755 mm). The product obtained was apparently a complex mixture of dimers and oxidation products, which was difficult to resolve owing to the negligible yield.

Under the conditions of synthesis diethyl ether was vigorously oxidized (cf. [5]). The acetaldehyde formed was identified in the form of the 2,4-dinitrophenylhydrazone; a mixed sample of the latter with the 2,4-dinitrophenylhydrazone of pure acetaldehyde, gave no melting point depression. The acetaldehyde was partially oxidized to acetic acid. The latter was identified through the formation of cacodyl oxide [14] and quantitatively determined by distillation and titration. There was found 0.135 mole of acetic acid. Apparently acetic acid was formed in the oxidation of acetaldehyde by Fe^{3+} ions, which was indicated by the change of color, on brief standing, of the water layer from light-brown to the light-green, characteristic of Fe^{2+} ions.

Dimerization of esters. Ethyl acetate. To a reaction mixture consisting of 700 ml of water and 250 ml of ethyl acetate, aqueous ferrous sulfate and hydrogen peroxide solutions (each 0.66 mole) were added during 10 min, with vigorous stirring. A temperature of 20-25° was maintained in the reaction flask by means of an ice bath. The organic layer (120 ml) was separated and the water layer extracted with diethyl ether. The combined organic layer and ethereal extracts were washed and dried. After distillation there was obtained 2 g of a dimer boiling in the interval 90-160° (10 mm), which was a clear, greenish liquid corresponding in its physical constants to isomeric diesters having the general formula $C_8H_{14}O_4$.

An aliquot part of the water layer was treated several times with diethyl ether in order to extract the dissolved ethyl acetate. Acetic acid was determined in the organic layer and the ethereal extract by titration, and in the water layer by distillation and subsequent titration. There was found 0.883 mole of acetic acid. Acetaldehyde, being an oxidation product of ethyl acetate [5], was identified in the form of the 2,4-dinitrophenylhydrazone (a mixed sample gave no melting-point depression). The somewhat large amount of acetic acid in comparison with the hydrogen peroxide taken is apparently explained by partial oxidation of the acetaldehyde.

n-Butyl acetate. To a mixture of 1000 ml of water, 500 ml of distilled n-butyl acetate, and 25 ml of concentrated sulfuric acid at room temperature, equivalent amounts of ferrous sulfate and hydrogen peroxide solutions (each 0.66 mole) were simultaneously added during 10 min, with vigorous stirring. At the end of the addition the reaction mass was stirred for 10 min more. The organic layer (475 ml) was separated. There were obtained 5.7 g of a colorless, viscous oil boiling at 95-155° (1 mm) and 3.7 g of a very viscous, dark residue. The latter was distilled from a small retort in vacuo (0.5 mm). A 2.2 g quantity of a very viscous, deep-yellow oil was collected. The 95-155° fraction (1 mm) corresponded in its physical constants to a mixture of isomeric diacetates having the general formula $C_{12}H_{22}O_4$ (see table). The molar weight of the heavier fraction (2.2 g) indicated that it consisted mainly of tetramers $C_{24}H_{48}O_8$. The tarry residue (1.5 g) apparently consisted of polymeric esters. The total quantity of organic acids, determined as described above, was 0.22 mole. The oxidation product of n-butyl acetate – n-butyraldehyde – was distilled from the organic layer in a fractionating column and identified in the form of the 2,4-dinitrophenylhydrazone. M.p. 122°. According to literature data: m.p. 122° [15].

Found %: C 48.20; H 4.55. $C_{10}H_{12}O_4N_4$. Calculated %: C 47.62; H 4.78.

Isoamyl acetate. The oxidative dimerization of isoamyl acetate was carried out as described for n-butyl acetate. The ferrous sulfate and hydrogen peroxide solutions were added to a mixture consisting of 1000 ml of water, 300 ml of isoamyl acetate, and 20 ml of concentrated sulfuric acid. The volume of the organic layer was 285 ml. There were obtained 5 g of a viscous, yellow liquid boiling at 50-134° (1 mm), and 0.7 g of a very viscous, reddish oil boiling above 134° (1 mm). The first fraction corresponded in its constants to diacetates having the formula $C_{14}H_{26}O_4$; the second fraction, judging from the molecular weight, consisted mainly of tetramers $C_{28}H_{50}O_8$. The total quantity of organic acids was 0.134 mole. The oxidation product of isoamyl acetate – isovaleraldehyde – was identified in the form of the 2,4-dinitrophenylhydrazone. M.p. 118°. According to literature data [15]: m.p. 123°

Found %: C 49.91; H 4.98. $C_{11}H_{14}O_4N_4$. Calculated %: C 49.63; H 5.30.

Isoamyl formate. The conditions of synthesis were similar to those for n-butyl acetate. The ferrous sulfate and hydrogen peroxide solutions were added to a mixture consisting of 1000 ml of water, 400 ml of isoamyl formate, and 25 ml of concentrated sulfuric acid. The volume of the organic layer was 385 ml. There were obtained 7 g (9.3%) of a product boiling in the interval 58-144° (2.5 mm), and 2.7 g of a viscous, tarry residue having the molecular weight 750. The 58-144° (2.5 mm) fraction was redistilled. There were obtained 5.4 g of a viscous, light-yellow product corresponding in its physical constants to the diformates of isomeric decanediols, and 1.28 g of a very viscous, deep-yellow oil, apparently consisting mainly of tetramers.

SUMMARY

It was found that organic radicals formed on interaction of aliphatic ethers and esters containing n carbon atoms, with free hydroxyl radicals, dimerize, forming diethers and diesters containing 2 n carbon atoms. The oxidation of the aliphatic ethers (or esters) to the corresponding carbonyl compounds is a competing reaction.

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THERMAL DECOMPOSITION OF TETRAETHYLLEAD, HEXAETHYLDIPLUMBANE, AND THEIR ANALOGS

IV. EFFECT OF PRECIPITATED LEAD, THE WALLS OF THE VESSEL, AND CERTAIN OTHER FACTORS ON THE DECOMPOSITION PROCESS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4099-4104, December, 1960
Original article submitted January 8, 1960

Earlier [1] we showed that the liquid-phase thermal decomposition of tetraethyllead is a complex chain process in which less-ethylated, intermediate compounds – hexaethyldiplumbane and diethyllead – are formed.

$$(C_2H_5)_4Pb \longrightarrow (C_2H_5)_6Pb_2 \longrightarrow (C_2H_5)_2Pb \longrightarrow Pb \qquad (1)$$

Moreover, a peculiarity of the reaction under consideration is the appearance of a solid phase – metallic lead. Since it is generally known that metal powders can catalyze the decomposition of organometallic compounds [2-4], it was of interest to study the role of highly-dispersed lead in complex conversions (I). In the literature we could not find direct experimental proof of the catalytic action of lead on the decomposition of tetraethyllead and hexaethyldiplumbane. Besides, a hypothesis of this kind was advanced by Berlin, who showed that the over-all process of thermal decomposition of tetraethyllead, which was followed by means of the evolved gas, is autocatalytic. Furthermore, Kothon found, in the case of tetraphenyllead, that metallic lead can accelerate the decomposition of organometallic compounds [5]. According to the author's data, the catalytic activity of lead strongly depends on the method of its preparation. This observation impelled us to abandon our attempts to introduce artificially prepared lead powders into tetraethyllead or hexaethyldiplumbane in order to determine their catalytic action.

In order to study the role of metallic lead in complex processes of thermal decomposition, we used data obtained earlier (Fig. 1) on the decomposition kinetics of binary mixtures of tetraethyllead and hexaethyldiplumbane [6]. As is evident from Fig. 1, in the decomposition of pure tetraethyllead the hexaethyldiplumbane concentration reaches some limiting value, characteristic for the given temperature (point A), after which it decreases. It was to be expected that in the decomposition of artificial mixtures of tetraethyllead and hexaethyldiplumbane with a concentration of the second component, close to the limiting value (point B), the kinetic curve would consist only of the descending branch. In this case, however, the beginning of decomposition is characterized by an increase in the hexaethyldiplumbane concentration.

On the basis of these facts it could be presumed that lead catalyzes the decomposition of the intermediate breakdown products, since hexaethyldiplumbane accumulates in its absence (point B), whereas in the presence of considerable quantities of the highly dispersed metal (point A) the $(C_2H_5)_6Pb_2$ concentration decreases.

The procedure was set forth in detail earlier [6]. In general it amounted to the distillation of previously purified tetraethyllead from a Claisen flask into a large ampule, to which a series of small ampules were sealed along its length. This operation was carried out in a current of hydrogen and at reduced pressure. Toward the

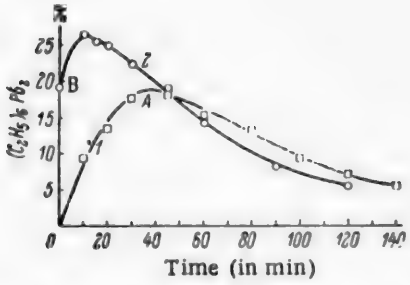

Fig. 1. Change of hexaethyldiplumbane concentration in tetraethyllead (wt. %) in the process of thermal decomposition at 135 ± 0.3°: 1) of pure tetraethyllead; 2) of a mixture of 19.2% hexaethyldiplumbane and 80.8% tetraethyllead.

Fig. 2. Ampule for studying the catalytic action of precipitated lead.

end of the distillation the pressure was reduced to 0.5-1.0 mm, and the system of ampules, which had the form of a comb, was sealed off in a current of hydrogen. Then the tetraethyllead was distributed among the small ampules, and they were sealed off from the main body. This method was used in all the experiments described below. The method made it possible to obtain simultaneously 10-12 ampules filled with an organolead compound of the same quality, free from oxidation products and out of contact with atmospheric oxygen. Several steps (construction of the apparatus from one batch of glass, and the like) were taken to ensure that the compound under investigation would be under strictly comparable conditions in all ampules of the series. All the above ensured quite satisfactory reproducibility of results. The latter was especially good in work with ampules of a single series.

In the case under discussion the series of small ampules had a complex configuration (see Fig. 2). All ampules were thermostated at 135 ± 0.3° for 35 min and then placed in liquid nitrogen. It was found spectrophotometrically [7] that, in conformity with Fig. 1, the hexaethyldiplumbane concentration in the reaction mixture becomes close to the limiting value in this case. Then the ampules were treated in two ways. After freezing, part of them were further thermostated at the same temperature for some time. Then these ampules were opened, the lead filtered out of the reaction mixture, and the latter analyzed in the usual way [7] for the hexaethyldiplumbane content in the tetraethyllead. The rest of the ampules were frozen and, without opening, the liquid part of the reaction mixture was decanted from the metallic lead and transferred to compartment B. In several well-reproducible experiments it was found that the composition of the mixture did not change during its decantation into compartment B. Then each compartment B was sealed off, further thermostated, and the contents analyzed for hexaethyldiplumbane Experimental results are given in Table 1.

From the experimental procedure it is evident that before the additional heating, the composition of the reaction mixtures in the two groups of ampules differed only by the presence or absence of metallic lead. Therefore the explanation of the differences in the compositions of the mixtures after additional heating must be sought in the changes introduced by highly dispersed lead in the thermal-decomposition process.

From the data of Table 1 it is evident that removal of lead from the reaction mixture leads to accumulation of the intermediate decomposition product, hexaethyldiplumbane. On the other hand, the concentration of this product decreases considerably in the presence of lead. These facts agree well with the results obtained earlier (see Fig. 1), and indicate decomposition of hexaethyldiplumbane on the precipitated lead; therefore the decomposition of tetraethyllead and hexaethyldiplumbane may be regarded as autocatalytic processes.

The procedure set forth above was used also to study the role of precipitated lead in the thermal decomposition of hexaethyldiplumbane. Earlier [1] we found that this substance decomposes with the intermediate formation of diethyllead according to the equations:

$$(C_2H_5)_3Pb{-}Pb(C_2H_5)_3 \longrightarrow (C_2H_5)_4Pb + (C_2H_5)_2Pb \qquad \text{(II)}$$

$$(C_2H_5)_2Pb \longrightarrow Pb + 2C_2H_5\cdot. \qquad \text{(III)}$$

TABLE 1

Quantity of hexaethyldiplumbane (%) in the main thermostating (135°, 35 min)	Additional thermostating at 135°	
	duration (in min)	quantity of hexaethyldiplumbane (%)
16.2	15	14.5
16.2	15	13.3
16.2	15	13.8
16.2	15*	20.7
16.2	15*	20.9
16.2	15*	20.1
16.2	15*	20.3
18.1**	10	17.0
18.1**	10*	19.7

*The mixture was separated from the metallic lead and transferred to compartment B before thermostating.

**Experiments with a second series of ampules.

Then it was found [6] that the decomposition kinetics of binary mixtures of hexaethyldiplumbane and diethyllead repeat the regularities of the decomposition kinetics of mixtures of tetraethyllead and hexaethyldiplumbane. In the decomposition of mixtures of this kind there was obtained, in particular, a picture analogous in many ways to that expressed in Fig. 1. Hence it appeared possible to find out whether precipitated lead would catalyze the decomposition of diethyllead. For this purpose we prepared a series of evacuated ampules like that shown in Fig. 2, filled with hexaethyldiplumbane by the method described earlier [6]. The ampules were thermostated at 85 ± 0.2° for 25 min and frozen in liquid nitrogen. In this case, in conformity with the preceding work, the reaction mixture acquired the maximum optical density for the given decomposition temperature, and also, therefore, the highest diethyllead concentration. Then part of the ampules were further thermostated with metallic lead. The liquid decomposition products in each of the rest of the ampules were first separated from highly dispersed lead by centrifuging, and then transferred to compartment B. Each compartment B was sealed off and further thermostated. Then the optical densities of the reaction mixtures in both groups of ampules were measured at the wavelength $\lambda = 400$ mμ, the thickness $\underline{d}$ of the absorbing layer being 0.020 mm (see Table 2).

TABLE 2

Optical densities of reaction mixtures

before thermostating	after the main thermostating (25 min at 85°)	after additional thermostating at 85° for		
		4 min	7 min	10 min
0.485	0.960	0.820	0.840	0.780
0.485	0.960	0.960*	0.980*	0.990*

*The mixture was separated from the metallic lead and transferred to compartment B before thermostating.

It follows from the data of Table 2, that the role of metallic lead in the decomposition of hexaethyldiplumbane is analogous to its role in the decomposition of tetraethyllead. And in this case further heating of the ampules containing metallic lead leads to a decrease in the concentration of the intermediate decomposition product (diethyllead), which is manifested in an appreciable decrease of optical density. On the other hand, removal of the lead before additional thermostating leads to an increase of optical density, or in other words, the accumulation of diethyllead. Since it was found that the composition of the liquid reaction products before additional heating is practically the same in both groups of ampules, and the optical-density measurement error was not over 0.020 in the worst case, we could find no other explanation of the observed phenomena.

The above-described facts with regard to the catalytic action of the solid phase on the decomposition of organolead compounds made it necessary for us to investigate the role of the wall on the thermal decomposition of these compounds and to estimate the degree of its influence on the process. For this purpose we prepared, in the usual way, a series of three groups of evacuated molybdenum-glass ampules filled with tetraethyllead. One-third of the ampules were intended for testing the quality of the tetraethyllead. Another third were filled with

TABLE 3

Duration of thermostating (in min)	Ampules without glass		Ampules with glass		$(C_2H_5)_4Pb$ kept beforehand over glass	
	$(C_2H_5)_4Pb_2$ (%)	Pb (%)	$(C_2H_5)_4Pb_2$ (%)	Pb (%)	$(C_2H_5)_4Pb_2$ (%)	Pb (%)
15	12.4	7.7	10.6	6.9	12.1	7.4
	12.6	8.1	11.2	7.3	13.4	7.9
	13.0	—	12.7	8.3	—	—
Average value	12.7	7.9	11.5	7.5	12.7	7.6
25	16.8	10.0	14.0	12.1	17.1	—
	17.0	12.8	15.8	11.8	17.6	—
	17.5	12.9	15.9	12.8	—	—
Average value	17.1	12.2	15.2	12.2	17.3	—

crushed molybdenum glass with a particle diameter of about 0.5 mm. The rest of the ampules had a complex configuration (see Fig. 2), compartment A containing crushed glass of the same dispersity. These ampules were intended for finding out whether crushed glass would introduce any impurities into the product being investigated. To determine this, tetraethyllead was digested for 8 hr over the crushed glass in each ampule, after which it was transferred to compartment B. Then each compartment B was sealed off and thermostated. All three groups of ampules were thermostated at 135° for 15 or 25 min, after which the metallic lead was filtered out, thoroughly washed with ether, and dissolved in nitric acid. The solution obtained was analyzed for lead by the molybdate method. After removal of the lead the liquid parts of the reaction mixtures were analyzed for hexaethyldiplumbane by a spectrophotometric method. Results of the analyses are given in Table 3.

It follows from the data of Table 3, that a considerable increase in the surface area of the glass has no substantial effect on the thermal decomposition process. This conclusion is confirmed by the wholly satisfactory reproducibility of results, observed by us during prolonged systematic investigations of the thermal decomposition of tetraethyllead. An analogous series of experiments was carried out with hexaethyldiplumbane. In this case also, however, we could not find any significant catalytic action of the wall.

On the other hand, products of incomplete oxidation of tetraethyllead and hexaethyldiplumbane, as well as incompletely removed atmospheric oxygen, cause sharp changes in the process of thermal decomposition of the compounds under investigation. In Fig. 3 are given data on the decomposition kinetics of pure tetraethyllead, as well as tetraethyllead in contact with atmospheric oxygen (1.0% by weight of the product sample taken). As is evident from Fig. 3, in cases where oxidation and thermal decomposition can compete, the first process completely suppresses the second. As a result, only oxidation products are precipitated in ampules containing atmospheric oxygen, after thermostating at 135 ± 0.3° for 15 min. The thermal-decomposition products—metallic lead and hexaethyldiplumbane—could not be detected. After the same time interval in ampules not containing oxygen, a considerable amount of lead and liquid decomposition products accumulated. The existence of an induction period in the decomposition of tetraethyllead in the presence of small amounts of oxygen indicates that this process is inhibited by oxidation products.

Small admixtures (up to 2.0 wt.%) of dibromoethane and other alkyl halides are even stronger inhibitors of the thermal decomposition of tetraethyllead.* Thus, for instance, a series of ampules containing a mixture of 98.5% tetraethyllead and 1.5% dibromoethane were successively thermostated for 5 hr at 135°, 4 hr at 145°, and finally 4 hr at 155° without formation of the metal or liquid decomposition products. As is well known [1], the pure product begins to decompose appreciably at 95-105°. During the thermostating of the above-mentioned mixture, triethyllead bromide was formed and lead bromide precipitated.

Since dibromoethane reacts quite vigorously with tetraethyllead even at 135°, it could be assumed that the inhibitor of thermal decomposition is not the alkyl halide itself, but products of its reaction with the organolead

*This part of the work was done by Yu. I. Dergunov.

compound. In order to test this hypothesis we studied the decomposition of a mixture of 99.2% tetraethyllead and 0.8 wt.% triethyllead bromide at 135 ± 0.3°. It was found that metallic lead did not separate from the mixture within 6 hr in this case. During the thermostating, white suspended matter formed, which contained lead and bromine. Then highly dispersed lead began to precipitate. After thermostating for 7.5 hr the degree of decomposition (according to the amount of metal formed) reached 12.9%. In the reaction mixture 3.2% hexaethyldiplumbane was found spectrophotometrically. At this time the solution contained practically no triethyllead bromide, as was proved by extracting the mixture with aqueous potassium hydroxide and analyzing the extract for bromide ion. As a rule, the analysis for bromide ion became negative as soon as metallic lead appeared. The mechanism of inhibition by triethyllead bromide is the subject of further investigations.

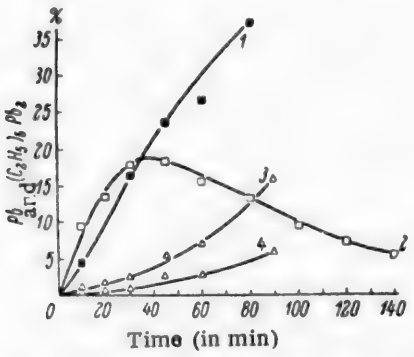

Fig. 3. Effect of atmospheric oxygen on the decomposition of tetraethyllead at 135 ± 0.3°. 1 and 3) Percentage of Pb formed; 2 and 4) change of hexaethyldiplumbane concentration in tetraethyllead; Curves 1 and 2 characterize decomposition without access of air; Curves 3 and 4 describe decomposition in the presence of 1.0 wt. % oxygen.

SUMMARY

1. It was found that in the thermal decomposition of tetraethyllead the final product (highly dispersed metallic lead) catalyzes the decomposition of the intermediate breakdown products—hexaethyldiplumbane and diethyllead. On this basis the thermal decomposition of tetraethyllead and hexaethyldiplumbane may be regarded as autocatalytic processes.

2. It was shown that the walls of the vessel have no substantial effect on the decomposition of tetraethyllead and hexaethyldiplumbane.

3. It was found that in the presence of atmospheric oxygen the oxidation of tetraethyllead completely suppresses the thermal decomposition reaction. Traces of atmospheric oxygen and products of the incomplete oxidation of tetraethyllead inhibit its thermal decomposition to a considerable degree.

4. The thermal decomposition reaction is more strongly inhibited by admixtures (up to 2 wt %) of alkyl halides or products of their interaction with tetraethyllead (e.g., triethyllead bromide).

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SYNTHESIS OF CERTAIN UNSYMMETRICAL THIURAM SULFIDES CONTAINING ALIPHATIC AND HETEROCYCLIC GROUPINGS IN THE MOLECULE

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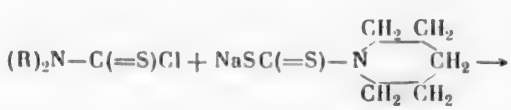
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4104-4107, December, 1960
Original article submitted January 3, 1960

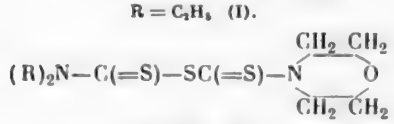
Thiuram sulfides may be prepared most simply from the corresponding thiuram disulfides by heating with potassium cyanide in aqueous alcoholic solutions [1]. However, this method is suitable mainly for preparing symmetrical thiuram sulfides. As regards the preparation of unsymmetrical thiuram sulfides, they are formed from salts of N-substituted dithiocarbamic acids with secondary amines or from water-soluble N-substituted alkali-metal dithiocarbamates by interaction with the corresponding N-substituted thiocarbamoyl chlorides [2].

In the course of searching for efficient accelerators of the sulfur vulcanization of natural and synthetic rubbers we synthesized unsymmetrical thiuram sulfides containing various aliphatic and heterocyclic groupings in the molecule. In the literature there is only one reference [3] to such compounds: in connection with a study of the toxicity of drugs, dimethylthiocarbamoyl-1-piperidinothiocarbonyl sulfide and dimethylthiocarbamoyl-4-morpholinothiocarbonyl sulfide are mentioned; in this case no information is given on the method of their preparation.

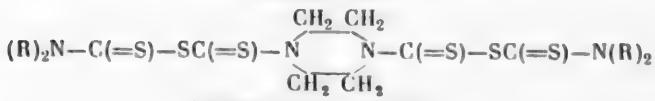
We prepared four hitherto-unknown substances: diethylthiocarbamoyl-1-piperidinothiocarbonyl sulfide (I), diethylthiocarbamoyl-4-morpholinothiocarbonyl sulfide (II), bis(dimethylthiocarbamoyl)-1,4-piperazinobis(thiocarbonyl) sulfide (III), and bis(diethylthiocarbamoyl)-1,4-piperazinobis (thiocarbonyl) sulfide (IV). The indicated compounds were prepared through the interaction in an aqueous medium of dimethyl- or diethylthiocarbamoyl chloride with sodium piperidine-1-carbodithioate, morpholine-4-carbodithioate, and piperazine-1,4-bis-(carbodithioate), respectively.



$R = C_2H_5$ (I).



$R = C_2H_5$ (II).



$R = CH_3$ (III), C_2H_5 (IV).

Dimethyl- or diethylthiocarbamoyl chloride was prepared from tetramethyl- or tetraethylthiuram disulfide respectively, by treatment with chlorine at a low temperature in a carbon tetrachloride medium.

EXPERIMENTAL

Diethylthiocarbamoyl-1-piperidinothiocarbonyl sulfide (I). Into a round-bottom flask provided with a mercury seal, reflux condenser, dropping funnel, and thermometer, 42.5 g of piperidine and 125 ml of 10% sodium hydroxide were put. The reaction mixture was cooled to 8-10°, and 38 g of carbon disulfide was slowly added during 1 hr, with stirring, after which the mixture was kept at 18-20° for 30 min. The precipitated sodium piperidine-1-carbodithioate dissolved on addition of 300 ml of water to the reaction mass, after which 75.5 g of powdered diethylthiocarbamoyl chloride (m.p. 45-46.5°) was added in small portions at 20-25°. Toward the end of the chloride addition the temperature was gradually raised to 60-65°, and the mixture was kept under these conditions for 1 hr. The oily product formed in the reaction was extracted with benzene. The extract was washed with water, the benzene then distilled off in vacuo (10-12 mm), and the product dried to constant weight over phosphorus pentachloride. Compound (I), an oily, yellow liquid, was obtained in a 110 g (80%) yield. It was insoluble in water, but readily soluble in cold benzene.

Found %: C 47.75; H 7.54; N 10.21; S 34.45. M 280. $C_{11}H_{20}N_2S_3$. Calculated %: C 47.82; H 7.24; N 10.14; S 34.78. M 276.

Diethylthiocarbamoyl-4-morpholinothiocarbonyl sulfide (II). This substance was synthesized under conditions similar to those of the preparation of (I); in this case the amounts of caustic alkali and water required for solution of the precipitated sodium morpholine-4-carbodithioate also were the same as those stated above. A 43.5 g quantity of morpholine, 38 g of carbon disulfide, and 75.5 g of diethylthiocarbamoyl chloride were taken. Compound (II) was a deep-yellow, oily liquid. Yield 105.5 g (76%). The substance was insoluble in water, but readily soluble in cold benzene.

Found %: C 43.8; H 6.37; N 10.10; S 34.0. M 282. $C_{10}H_{18}ON_2S_3$. Calculated %: C 43.16; H 6.47; N 10.07; S 34.53. M 278.

Bis(dimethylthiocarbamoyl)-1,4-piperazinobis(thiocarbonyl) sulfide (III). This substance was prepared under the conditions described for the synthesis of (I), using the same quantities of sodium hydroxide and water to dissolve the precipitated disodium piperazine-1,4-bis(carbodithioate). A 21.5 g quantity of piperazine (in the form of the free base), 38 g of carbon disulfide, and 62 g of dimethylthiocarbamoyl chloride, m.p. 43-44°, were taken. The yellow, crystalline precipitate resulting from the reaction was filtered out, washed with water and alcohol, and dried to constant weight. Yield 64.8 g (63%). The substance did not melt up to 250°; on heating above this temperature it darkened and partly decomposed. Substance (III) was insoluble on heating in water, ether, alcohol and carbon tetrachloride and very slightly soluble in hot benzene and dichloroethane.

Found %: C 34.75; H 5.09; N 13.91; S 46.75. $C_{12}H_{20}N_4S_6$. Calculated %: C 34.95; H 4.85; N 13.59; S 46.60.

Bis(diethylthiocarbamoyl)-1,4-piperazinobis(thiocarbonyl) sulfide (IV). This substance was synthesized like (III). A 21.5 g quantity of piperazine, 38 g of carbon disulfide, and 75.5 g of diethylthiocarbamoyl chloride were taken. The light-yellow, crystalline precipitate resulting from the reaction was washed and dried, after which it did not melt on heating up to 250°. Yield 74.5 g (64%). The substance was insoluble on heating in water, alcohol, ether, and carbon tetrachloride and very slightly soluble in hot benzene and dichloroethane.

Found %: C 41.25; H 6.00; N 12.12; S 40.97. $C_{16}H_{28}N_4S_6$. Calculated %: C 41.02; H 5.99; N 11.95; S 41.03.

SUMMARY

Four unsymmetrical thiuram sulfides, not previously described in the literature, were synthesized: diethylthiocarbamoyl-1-piperidinothiocarbonyl sulfide, diethylthiocarbamoyl-4-morpholinothiocarbonyl sulfide, bis(dimethylthiocarbamoyl)-1,4-piperazinobis(thiocarbonyl) sulfide, and bis(diethylthiocarbamoyl)-1,4-piperazinobis(thiocarbonyl) sulfide. These compounds were prepared through the interaction of piperidine, morpholine, and piperazine with carbon disulfide in an aqueous-alkaline medium, followed by condensation of the resulting intermediate sodium salts of the corresponding carbodithioic acids, with dimethyl- or diethylthiocarbamoyl chloride.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. ***Some or all of this periodical literature may well be available in English translation.*** **A complete list of the cover-to-cover English translations appears at the back of this issue.**

LETTERS TO THE EDITOR

USE OF ETHYL MONOFLUOROACETATE IN THE DARZENS REACTION

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4107-4108, December, 1960
Original article submitted June 1, 1960

The Darzens reaction has been known for more than 50 years; however, its mechanism is discussed in the literature even now. On the basis of a number of facts it must be presumed that the reaction is an aldol-type process in which intermediate hydroxyhalogen compounds are formed; when the reaction is carried out under ordinary conditions, the latter cannot be isolated, since the hydroxyhalogen compounds are rapidly converted to the corresponding epoxy compounds under the reaction conditions (alkaline medium). It proved possible to recover the intermediate compounds in only two cases [1, 2], by carrying out the reaction under special conditions.

Chloro or bromo derivatives are usually used in the Darzens reaction. We used fluoro derivatives for the first time, namely, ethyl monofluoroacetate, which was condensed with benzaldehyde. It is well known that fluorine is much more stable to S_{N2} substitution; hence we assumed that, if the Darzens reaction is an aldol-type process, the fluorohydrin which must appear in this case will not be converted further to the corresponding epoxy compound.

$$C_6H_5-C\begin{matrix}O\\H\end{matrix} + HFCH-COOC_2H_5 \xrightarrow{NaOC_2H_5} C_6H_5-CHOH-CHF-COOC_2H_5$$

We condensed ethyl monofluoroacetate with benzaldehyde in the presence of dry sodium ethoxide under the usual conditions for this synthesis, without any precautions. Absolute ether was used as solvent. The reaction mass was decomposed with water acidified with H_2SO_4. A liquid substance with b.p. 121-123° (7 mm) was isolated from the ethereal extract, whereas a crystalline compound with m.p. 153° was obtained from the water layer. According to its molecular weight and analyses for carbon, hydrogen, and fluorine, the latter corresponded to α-fluoro-β-hydroxy-β-phenylpropionic acid. It contained two active hydrogen atoms and was titrated with alkali. Yield 20%.

Found %: C 58.99; H 4.93; F 10.37; OH 18.45. M 187. $C_9H_9O_3F$. Calculated %: C 58.70; H 4.89; F 10.32; OH 18.48. M 184.

Apparently, ethyl α-fluoro-β-hydroxy-β-phenylpropionate was hydrolyzed in the course of synthesis or isolation.

The liquid product contained fluorine but did not show a reaction for an active hydrogen atom. According to the molecular weight and analytical data for carbon, hydrogen, and fluorine, this compound corresponded to ethyl α-fluorocinnamate. Yield 19.7%.

$n^{20}D$ 1.5412, d^{20}_4 1.130.

Found %: C 67.83; H 5.84; F 9.77. M 185. $C_{11}H_{11}O_2F$. Calculated %: C 68.04; H 5.67; F 9.79; M 194.

This compound could be formed through splitting-out of a water molecule from ethyl α-fluoro-β-hydroxy-β-phenylpropionate.

$$C_6H_5CHOH—CHF—COOC_2H_5 \xrightarrow{-H_2O} C_6H_5—CH=CF—COOC_2H_5$$

The formation of such compounds in small amounts is observed very often in Darzens condensations.

The results obtained by us, in our opinion, prove conclusively that the Darzens reaction goes by an aldol-type mechanism.

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SULFIDES CONTAINING LACTAM RINGS

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4108-4109,
December, 1960
Original article submitted July 11, 1960

Independently of the authors of the recently published work [1], we prepared N-allyl-α-pyrrolidone (I), N-allyl-ε-caprolactam (II), and, for the first time, N-allyl-α-piperidone (III) through the interaction of lactam Na salts and allyl halides, and studied their polymerization and the copolymerization of (I) with methyl methacrylate and methyl acrylate [2]. The subject of the present letter is the addition, studied for the first time, of mercaptans to (I) and (II) and to N-vinyllactams.

When (I) and (II) are heated with equimolar quantities of ethyl mercaptan (IV), n-butyl mercaptan, and ethyl thioglycolate (V) in the presence of azoisobutyric dinitrile (0.5% of the total weight) in an ampule at 70-80° for 18 hr, compounds having the general formula $\overbrace{(CH_2)_n CO-N}-(CH_2)_3SR$ are obtained in 65-88% yield. Thiophenol (VI) adds with difficulty under the indicated conditions, and after heating for 45 hr gives traces of high-boiling products, the original compounds being recovered. For the compounds obtained we give: the value of n, the value of R, yield (in %), boiling point (pressure in mm), $n^{20}D$, d^{20}_4.

5, C_2H_5, 80.5, 129—131° (1), 1.5140, 1.0401 (VII); 3, C_2H_5, 65, 154—155° (5), 1.5120, 1.0602 (VIII); 5, n-C_4H_9, 79.8, 156.5—157° (1.5), 1.5070, 1.0154 (IX); 3, n-C_4H_9, 70, 142—143° (1.5), 1.5045, 1.0226 (X); 5, $CH_2COOC_2H_5$, 87.6, 118—121° ($5 \cdot 10^{-3}$), 1.5093, 1.1184 (XI); 3, $CH_2COOC_2H_5$, 85.7, 105—107° ($2.5 \cdot 10^{-3}$), 1.5067, 1.1420 (XII); 5, C_6H_5, 5.5, 170—173° (0.7), 1.5670 (XIII); 3, C_6H_5, 8.8, 210—212 (3), 1.5770, — (XIV).

Analytical data on the C, H, and S content in substances (VII-XII) correspond to the calculated values.

In order to compare the chemical activity of vinyl- and allyllactams under similar conditions (IV), (V), and (VI) were added to N-vinyl-α-pyrrolidone and N-vinyl-ε-caprolactam. For the $(CH_2)_n-CO-N-(CH_2)_2SR$ compounds obtained we give: the value of n, the value of R, yield (in %), boiling point (pressure in mm) $n^{25}D$, d^{25}_4.

5, $CH_2COOC_2H_5$, 91.5, 175° (0.5), 1.5085, 1.1336 (XV); 3, $CH_2COOC_2H_5$, 97.5, 165° (1), 1.5065, 1.1683 (XVI); 5, C_6H_5, 47.8, 181—183° (1), 1.5708,* m.p. 60—60.5° (XVII); 3, C_6H_5, 36.6, 161—163°(1), 1.5740, 1.1389 (XVIII); 5, C_2H_5, 56.5, 151.5° (3), 1.5150, 1.0587 (XIX); 3, C_2H_5, 57.8, 114—115° (0.5), 1.5132, 1.0749 (XX).

Analytical data on the C, H and S content in (XV-XX) correspond to the calculated values. The structure of (XVI) was proved by counter-synthesis from β-chloroethylpyrrolidone and $NaSCH_2COOC_2H_5$.

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*Supercooled liquid.

A NEW TYPE OF DISPROPORTIONATION

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Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, pp. 4109-4110,
December, 1960
Original article submitted July 12, 1960

In an attempt to condense acetoxymalonic ester with p-nitrobenzyl bromide in anhydrous ethanol in the presence of C_2H_5ONa (1 hr at 20-22° and 1 hr at 40°) we found that, instead of the expected p-nitrobenzylacetoxymalonic ester, the reaction gave bis-(p-nitrobenzyl)malonic ester, m.p. 169.5-170.5° (from benzene) [1] and mesoxalic ester (fraction with b.p. up to 130° at 20-21 mm), which were isolated; on addition of a little water the latter gave a crystalline hydrate, m.p. 59-60.5° (from alcohol) [2].

The results obtained indicate that under the given conditions there occurred simultaneous oxidation and reduction with formation of mesoxalic and malonic esters, the latter reacting with p-nitrobenzyl bromide in the presence of sodium ethoxide to give bis-(p-nitrobenzyl)-malonic ester.

Actually the reaction of acetoxymalonic ester alone, with a solution of sodium ethoxide in absolute ether under the same conditions gave a fraction with b.p. 103-110° at 19-20 mm, containing malonic ester. The latter was proved by its reaction with p-nitrobenzaldehyde in the presence of piperidine, which gave p-nitrobenzalmalonic ester, m.p. 91-92° (from alcohol) [3].

Most probably, it is not acetoxymalonic ester itself that disproportionates under these conditions, but tartronic ester, which could easily be formed as a result of transesterification under the influence of sodium ethoxide.

$$CH_3COOCH(COOC_2H_5)_2 + C_2H_5OH \xrightarrow{C_2H_5ONa} HOCH(COOC_2H_5)_2 + CH_3COOC_2H_5,$$
$$2HOCH(COOC_2H_5)_2 \longrightarrow CH_2(COOC_2H_5)_2 + CO(COOC_2H_5)_2$$

Thus the described reaction is a new type of oxidation-reduction conversion of secondary alcohols, taking place in an anhydrous medium in the presence of sodium ethoxide. Cases of similar behavior of such secondary alcohols as benzhydrol, p,p'-dimethoxybenzhydrol, and xanthydrol, described in the literature [4-6], are undoubtedly based on another mechanism, since these processes occur only in an acid medium.

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REACTION OF 2-FORMYLCYCLOHEXANONE WITH HYDROGEN PEROXIDE

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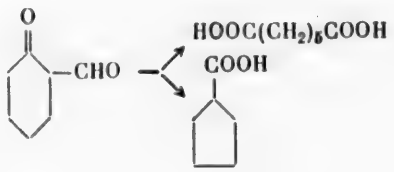
Translated from Zhurnal Obshchei Khimii, Vol. 30, No. 12, p. 4110, December, 1960
Original article submitted July 18, 1960

We found an interesting, new reaction of 2-formylcyclohexanone, similar to the Favorskii rearrangement but taking place under unusual conditions. On addition of 2-formylcyclohexanone to 30% hydrogen peroxide in the cold, considerable heating is observed, and pimelic and cyclopentanecarboxylic acids are formed as a result, the latter being obtained in about 40% yield.



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Soviet Journals Available in Cover-to-Cover Translation

ABBREVIATION	RUSSIAN TITLE	TITLE OF TRANSLATION	PUBLISHER	TRANSLATION BEGAN Vol.	Issue	Year
AÉ	Atomnaya énergiya	Soviet Journal of Atomic Energy	Consultants Bureau	1	1	1956
Akust. zh.	Akusticheskii zhurnal	Soviet Physics – Acoustics	American Institute of Physics	1	1	1955
	Antibiotiki	Antibiotics	Consultants Bureau	4	1	1959
Astr(on). zh(urn).	Astronomicheskii zhurnal	Soviet Astronomy–AJ	American Institute of Physics	34	1	1957
Avto(mat). svarka	Avtomaticheskaya svarka	Automatic Welding	British Welding Research Association (London)		1	1959
	Avtomatika i Telemekhanika	Automation and Remote Control	Instrument Society of America	27	1	1956
	Biofizika	Biophysics	National Institutes of Health*		1	1957
	Biokhimiya	Biochemistry	Consultants Bureau	21	1	1956
Byull. éksp(erim). biol. i med.	Byulleten' éksperimental'noi biologii i meditsiny	Bulletin of Experimental Biology and Medicine	Consultants Bureau	41	1	1959
DAN (SSSR) / Dokl(ady) AN SSSR	Doklady Akademii Nauk SSSR	The translation of this journal is published in sections, as follows:				
Life Sciences		Doklady Biochemistry Section	American Institute of Biological Sciences	106	1	1956
		Doklady Biological Sciences Sections (Includes: Anatomy, biophysics, cytology, ecology, embryology, endocrinology, evolutionary morphology, genetics, histology, hydrobiology, microbiology, morphology, parasitology, physiology, zoology sections)	American Institute of Biological Sciences	112	1	1957
		Doklady Botanical Sciences Sections (Includes: Botany, phytopathology, plant anatomy, plant ecology, plant embryology, plant physiology, plant morphology sections)	American Institute of Biological Sciences	112	1	1957
Chemical Sciences		Proceedings of the Academy of Sciences of the USSR, Section: Chemical Technology	Consultants Bureau	106	1	1956
		Proceedings of the Academy of Sciences of the USSR, Section: Chemistry	Consultants Bureau	106	1	1956
		Proceedings of the Academy of Sciences of the USSR, Section: Physical Chemistry	Consultants Bureau	112	1	1957
Earth Sciences		Doklady Earth Sciences Sections (Includes: Geochemistry, geology, geophysics, hydrogeology, mineralogy, paleontology, petrography, permafrost sections)	American Geological Institute	124	1	1959
		Proceedings of the Academy of Sciences of the USSR, Section: Geochemistry	Consultants Bureau	106-123	1-6	1957-1958
		Proceedings of the Academy of Sciences of the USSR, Sections: Geology	Consultants Bureau	106-123	1-6	1957-1958
Mathematics		Doklady Soviet Mathematics	The American Mathematics Society	131	1	1961
Physics		Soviet Physics–Doklady (Includes: Aerodynamics, astronomy, crystallography, cybernetics and control theory, electrical engineering, energetics, fluid mechanics, heat engineering, hydraulics, mathematical physics, mechanics, physics, technical physics, theory of elasticity sections)	American Institute of Physics	106	1	1956
		Proceedings of the Academy of Sciences of the USSR, Applied Physics Sections (does not include mathematical physics or physics sections)	Consultants Bureau	106-117	1	1956-1957
Derevoobrabat. prom-st'.	Derevoobrabatyvayushchaya promyshlennost'	Wood Processing Industry	Timber Development Association (London)		9	1959
Élektrosvyaz	Élecktrosvyaz	Telecommunications	Massachusetts Institute of Technology*		1	1957
Éntom(ol). oboz(renie)	Éntomologicheskoe obozrenie	Entomological Review	American Institute of Biological Sciences	38	1	1959
Farmakol. (i) toksikol(ogiya)	Farmakologiya i toksikologiya	Pharmacology and Toxicology	Consultants Bureau	20	1	1957
FMM	Fizika metallov i metallovedenie	Physics of Metals and Metallography	Acta Metallurgica*	5	1	1957
Fiziol. zhurn. SSSR (im. Sechenova)	Fiziologicheskii zhurnal im. I. M. Sechenova	Sechenov Physiological Journal USSR	National Institutes of Health*		1	1957
Fiziol(ogiya) rast.	Fiziologiya rastenii	Plant Physiology	American Institute of Biological Sciences	4	1	1957
	Geokhimiya	Geochemistry	The Geochemical Society		1	1958
FTT	Fizika tverdogo tela	Soviet Physics–Solid State	American Institute of Physics	1	1	1959
Izmerit. tekh(nika)	Izmeritel'naya tekhnika	Measurement Techniques	Instrument Society of America		1	1959
Izv. AN SSSR, O(td). Kh(im). N(auk)	Izvestiya Akademii Nauk SSSR: Otdelenie khimicheskikh nauk	Bulletin of the Academy of Sciences of the USSR: Division of Chemical Sciences	Consultants Bureau		1	1952

continued

Izv. AN SSSR, O(td). T(ekhn). N(auk): Met(all). i top.	(see Met. i top.)				
Izv. AN SSSR Ser. fiz(ich).	Izvestiya Akademii Nauk SSSR: Seriya fizicheskaya	Bulletin of the Academy of Sciences of the USSR: Physical Series	Columbia Technical Translations	1	1954
Izv. AN SSSR Ser. geofiz.	Izvestiya Akademii Nauk SSSR: Seriya geofizicheskaya	Bulletin (Izvestiya) of the Academy of Sciences USSR: Geophysics Series	American Geophysical Union	1	1954
Izv. AN SSSR Ser. geol.	Izvestiya Akademii Nauk SSSR: Seriya geologicheskaya	Izvestiya of the Academy of Sciences of the USSR: Geologic Series	American Geological Institute	1	1958
Kauch. i rez.	Kauchuk i rezina	Soviet Rubber Technology	Research Association of British Rubber Manufacturers	18	1 1959
	Kinetika i kataliz	Kinetics and Catalysis	Consultants Bureau	1	3 1960
	Koks i khimiya	Coke and Chemistry USSR	Coal Tar Research Association (Leeds, England)		1 1958
Kolloidn. zh(urn).	Kolloidnyi zhurnal	Colloid Journal	Consultants Bureau	14	1 1952
	Kristallografiya	Soviet Physics – Crystallography	American Institute of Physics	2	1 1957
Metalov. i term. obrabot. metal.	Metallovedenie i termicheskaya obrabotka metallov	Metal Science and Heat Treatment of Metals	Acta Metallurgica	6	1 1958
	Metallurg	Metallurgist	Acta Metallurgica		1 1957
Met. i top.	Metallurgiya i topliva	Russian Metallurgy and Fuels	Eagle Technical Publications		1 1960
Mikrobiol.	Mikrobiologiya	Microbiology	American Institute of Biological Sciences	26	1 1957
OS	Optika i spektroskopiya	Optics and Spectroscopy	American Institute of Physics		6 1959
	Pochvovedenie	Soviet Soil Science	American Institute of Biological Sciences		1 1958
	Priborostroenie	Instrument Construction	British Scientific Instrument Research Association		1 1959
Pribory i tekhn. éks(perimenta)	Pribory i tekhnika éksperimenta	Instruments and Experimental Techniques	Instrument Society of America		1 1957
Prikl. matem. i mekh.	Prikladnaya matematika i mekhanika	Applied Mathematics and Mechanics	American Society of Mechanical Engineers		1 1958
PTÉ	(see Pribory i tekhn. éks.)				
	Problemy Severa	Problems of the North	National Research Council of Canada		
Radiotekh.	Radiotekhnika	Radio Engineering	Massachusetts Institute of Technology*	12	1 1957
Radiotekh. i élektronika	Radiotekhnika i élektronika	Radio Engineering and Electronics	Massachusetts Institute of Technology*	2	1 1957
	Stanki i instrument	Machines and Tooling	Production Engineering Research Assoc.		1 1959
	Stal'	Stal (In English)	Iron and Steel Institute		1 1959
Stek. i keram.	Steklo i keramika	Glass and Ceramics	Consultants Bureau	13	1 1956
Svaroch. proiz-vo	Svarochnoe proizvodstvo	Welding Production	British Welding Research Association		4 1959
Teor. veroyat. i prim.	Teoriya veroyatnostei i ee primenenie	Theory of Probability and Its Applications	Society for Industrial and Applied Mathematics		1 1956
Tsvet. Metally	Tsvetnye metally	Nonferrous Metals	Primary Sources		1 1960
UFN	Uspekhi fizicheskikh Nauk	Soviet Physics – Uspekhi (partial translation)	American Institute of Physics	66	1 1958
UKh	Uspekhi khimii	Russian Chemical Reviews	The Chemical Society (London)		1 1960
UMN	Uspekhi matematicheskikh nauk	Russian Mathematical Surveys	London Mathematical Society	15	1 1960
Usp. fiz. nauk	(see UFN)				
Usp. khim(ii)	(see UKh)				
Usp. matem. nauk	(see UMN)				
Usp. sovr. biol.	Uspekhi sovremennoi biologii	Russian Review of Biology	Oliver and Boyd	48	1959
Vest. mashinostroeniya	Vestnik mashinostroeniya	Russian Engineering Journal	Production Engineering Research Assoc.	4	1959
Vop. gem. i per. krovi	Voprosy gematologii i perelivaniya krovi	Problems of Hematology and Blood Transfusion	National Institutes of Health*	1	1957
Vop. onk.	Voprosy onkologii	Problems of Oncology	National Institutes of Health*	1	1957
Vop. virusol.	Voprosy virusologii	Problems of Virology	National Institutes of Health*	1	1957
Zav(odsk). lab(oratoriya)	Zavodskaya laboratoriya	Industrial Laboratory	Instrument Society of America	25	1 1959
ZhAKh Zh. anal(it). khimii	Zhurnal analiticheskoi khimii	Journal of Analytical Chemistry USSR	Consultants Bureau	7	1 1952
ZhETF Zh. éksperim. i teor. fiz.	Zhurnal éksperimental'noi i teoreticheskoi fiziki	Soviet Physics–JETP	American Institute of Physics	28	1 1955
ZhFKh Zh. fiz. khimii	Zhurnal fizicheskoi khimii	Russian Journal of Physical Chemistry	The Chemical Society (London)		7 1959
ZhMÉI Zh(urn). mikrobiol. épidemiol. i immunobiol.	Zhurnal mikrobiologii, épidemiologii i immunobiologii	Journal of Microbiology, Epidemiology and Immunobiology	National Institutes of Health*		1 1957
ZhNKh Zh(urn). neorgan(ich). khim(ii)	Zhurnal neorganicheskoi khimii	The Russian Journal of Inorganic Chemistry	The Chemical Society (London)		1 1959
ZhOKh Zh(urn). obshch(ei) khimii	Zhurnal obshchei khimii	Journal of General Chemistry USSR	Consultants Bureau	19	1 1949
ZhPKh Zh(urn). prikl. khimii	Zhurnal prikladnoi khimli	Journal of Applied Chemistry USSR	Consultants Bureau	23	1 1950
ZhSKh Zh(urn). strukt. khimii	Zhurnal strukturnoi khimii	Journal of Structural Chemistry	Consultants Bureau	1	1 1960
ZhTF Zh(urn). tekhn. fiz.	Zhurnal teknicheskoi fiziki	Soviet Physics–Technical Physics	American Institute of Physics	26	1 1956
Zh(urn). vyssh. nervn. deyat. (im. Pavlova)	Zhurnal vysshei nervnoi deyatel'nosti (im. I. P. Pavlova)	Pavlov Journal of Higher Nervous Activity	National Institutes of Health*		1 1958

*Sponsoring organization. Translation through 1960 issues is a publication of Pergamon Press.

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Metrology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.